AN OBSERVATIONAL STUDY OF IRON CHELATION PRACTICES IN THALASSEMIA DAY CARE CENTRE OF A TERTIARY CARE HOSPITAL IN PUNJAB

A THESIS SUBMITTED TO BABA FARID UNIVERSITY OF

HEALTH SCIENCES, FARIDKOT (PUNJAB)

IN THE PARTIAL FULFILLMENT

FOR THE AWARD OF DEGREE OF

DOCTORATE OF MEDICINE

IN

PAEDIATRICS

2024

DR. VERONICA BANAL

DEPARTMENT OF PAEDIATRICS

DAYANAND MEDICAL COLLEGE & HOSPITAL

LUDHIANA, PUNJAB-141001

DECLARATION BY THE CANDIDATE

I hereby declare that the thesis entitled "**AN OBSERVATIONAL STUDY OF IRON CHELATION PRACTICES IN THALASSEMIA DAY CARE CENTRE OF A TERTIARY CARE HOSPITAL IN PUNJAB**" submitted towards partial fulfillment of the requirements for the award of **MD in Paediatrics** degree to BFUHS is a compilation of original work carried out by me under the supervision **Dr. Shruti Kakkar**, Associate Professor, Department of Paediatrics, **Dr. Deepak Bhat**, Professor, Department of Paediatrics and **Dr. Sandeep Kaushal**, Professor & Head, Department of Pharmacology. No part of this thesis has formed the basis for the award of any degree previously.

_____

Dr. VERONICA BANAL
MD Resident
Dept. of Paediatrics
DMC & Hospital, Ludhiana

Date:

Place:

CERTIFICATE OF SUPERVISORS

This is to certify that the work incorporated in this thesis entitled "**AN OBSERVATIONAL STUDY OF IRON CHELATION PRACTICES IN THALASSEMIA DAY CARE CENTRE OF A TERTIARY CARE HOSPITAL IN PUNJAB**" has been carried out by **Dr. Veronica Banal** under our direct supervision. The data incorporated in this thesis is original and genuine and has been carried out by the candidate herself.

Signature of Supervisor

Dr. Shruti Kakkar
Associate Professor
Department of Paediatrics
DMCH, Ludhiana

Signature of Co-Supervisors

Dr. Deepak Bhat
Professor
Department of Paediatrics
DMCH, Ludhiana

Dr. Sandeep Kaushal
Professor & Head
Department of Pharmacology
DMCH, Ludhiana

Date:

ENDORSEMENT BY THE HEAD OF THE INSTITUTE

This is to certify that the thesis "**AN OBSERVATIONAL STUDY OF IRON CHELATION PRACTICES IN THALASSEMIA DAY CARE CENTRE OF A TERTIARY CARE HOSPITAL IN PUNJAB**" is a bonafide research work done by **Dr. Veronica Banal** under the supervision **Dr. Shruti Kakkar**, Associate Professor, Department of Paediatrics, **Dr. Deepak Bhat**, Professor, Department of Paediatrics and **Dr. Sandeep Kaushal**, Professor & Head, Department of Pharmacology, in this institution.

Principal

Dr. G S Wander
Principal
DMC&H, Ludhiana

Date:

COPYRIGHT

Declaration by the Candidate

I hereby declare that the Baba Farid University of Heath Sciences, Faridkot, shall have the rights to preserve & use this thesis in print or electronic format for academic/study purpose by the research scholar/students.

Signature

Dr. Veronica Banal
MD Resident
Dept. of Paediatrics,
DMC & Hospital,
Ludhiana

Date:

© Baba Farid University of Health Sciences, Faridkot

Dedicated

to

My Family,

friends

&

Teachers

ACKNOWLEDGEMENT

I am highly grateful to the Almighty, without whose blessings no work can be conceived or completed. HIS presence we feel at every step of life. He's the one who holds our hands and guides us through everything. I take this opportunity to thank everyone who has been helping me in the successful completion of this work. With deep gratitude, I would like to thank my esteemed teacher and supervisor **Dr. Shruti Kakkar**, Associate Professor, Department of Paediatrics, DMC&H Ludhiana, who has been most helpful and supportive throughout my tenure. Her able and mature guidance, ever willing nature helped me to complete my task easily. She has always been the epitome of excellence for me. With great reverence and profound pleasure, I acknowledge the valuable suggestions by my co-supervisor **Dr. Sandeep Kaushal** Professor & Head, Department of Pharmacology, DMCH, Ludhiana and **Dr Deepak Bhat**, Professor, Department of Pediatrics, DMC&H Ludhiana.

Their constant encouragement throughout the whole time helped me a long way in completing this project. I want to offer my sincere thanks to Dr. Puneet A Pooni, Professor and Head of the Department of Pediatrics, DMC&H Ludhiana for her constant encouragement. I also wish to thank Dr. Kamal Arora, Dr. Gurdeep Singh Dhooria, Dr. Siddharth Bhargava, Dr. J.S. Goraya and Dr. Karambir Singh Gill. I am indebted to my seniors Dr Himanshu, Dr. Amneet, Dr. Mittali, Dr. Chandan and Dr. Akshay for their encouraging words, support, and guidance throughout the thesis. My heartiest thanks to my dear colleagues Dr. Lovepreet, Dr. Kirti,

Dr Amandeep, Dr. Mayank, Dr. Savi, and Dr. Asmita for their brilliant company in this journey. I want to thank to all my juniors especially Dr. Gagan, who have been an invaluable support day in, and day out for the entire work. Words are woefully inadequate to express my sense of gratitude to my parents, my in-laws and my brother Dr. Victor Banal for their love, selfless sacrifices, motivation, unfailing attention to my needs, and blessings that they have showered upon me. I am blessed to have

Mr. Yogesh Khinder as my husband to give his continuous support, encouragement, and affection which is extremely valuable to me. Thanks to all the children who have been a part of this study and their parents as well. I sincerely thank the nursing staff of our department; their unending help made this uphill task possible.

Dr. Veronica Banal

ABBREVIATIONS

TDT - Transfusion dependent Thalassemia

ICT - Iron Chelation Therapy

DFO - Deferoxamine

DFX - Deferasirox

DFP - Deferiprone

LIC - Liver iron concentration

MIC - Myocardial iron concentration

HbA - Adult hemoglobin

HbF - Fetal hemoglobin

ABSTRACT

Introduction: Thalassemia is a hereditary disorder, characterised by abnormal synthesis of hemoglobin molecules. Clinically, chronic blood transfusion is required for thalassemia patients to attenuate anaemia and increase the haemoglobin level. However, multiple episodes of blood transfusion to achieve these goals will increase systemic iron overload can lead to iron accumulation in the heart, liver, spleen, and other organs, which can cause a variety of complications. Thus, iron chelation therapy (ICT) is crucial to manage post-transfusional iron overload. To date, there are three iron chelators available in the market: deferoxamine (DFO), deferiprone (DFP), and deferasirox (DFX).

Aim of the study: To study iron chelation practices and compare iron overload outcomes across various treatment regimes in the thalassemia day care center of a tertiary care hospital in Punjab.

Material and methods: The study population included 148 TDT patients receiving regular blood transfusions and were on either single or combination iron chelation. The serial growth parameters like height, weight, SMR and iron overloading parameters like serum ferritin, MRI for cardiac iron overload and LIC were monitored and compared. The adverse effects caused by the drugs were evaluated. The comparison was then studied for each iron chelator's efficacy and safety profile.

Results – There was a rise in number of patients who enrolled over the years in the thalassemia unit and out of 148 patients, the average mean ferritin of the study population has decreased from 2566.88 ± 1480 ng/ml at the time of initiation of iron chelation at our unit to 2095.62 ± 1151.98ng/ml at the time of the last assessment. The mean cardiac MRI T2* at the time of assessment was 23.37 ms and at the year of last assessment (2022), A total of 52 out of 70 patients had MRI T2* value > 20 ms. The mean LIC was 5.18 mg/g dry weight of the liver at the time of assessment and at the year of last assessment (2022) a total of 23 out of 69 patients had LIC 7-15 mg/g dry weight. The most common adverse effect seen was GI disturbance followed by nausea and vomiting. Permanent with-drawl of the drug was required in only 4 patients out of all the study population.

Conclusion: Long-term treatment with all the three iron chelators is well tolerated and is safe and effective to reduce the iron overload in TDT patients. Most of the adverse events were manageable, but the safety and efficacy parameters should be continuously monitored. The outcome improves with improved compliance to ICT.

TABLE OF CONTENTS

S. NO.	TOPIC	PAGES
I	INTRODUCTION	1-4
II	AIMS AND OBJECTIVES	5
III	REVIEW OF LITERATURE	6-14
IV	MATERIALS AND METHODS	15-18
V	OBSERVATIONS AND RESULTS	19-63
VI	DISCUSSION	64-71
VII	SUMMARY AND CONCLUSION	72-74
VIII	BIBLIOGRAPHY	75-81

APPENDICES – I

- PROFORMA
- MASTER CHART

APPENDICES – II

- APPROVAL LETTER OF THESIS PLAN
- THESIS PLAN

LIST OF TABLES

Table No.	Title	Page No.
1.	Iron chelators and their properties	4
2.	Investigation and frequency	15
3.	Lab investigation and frequency	16
4.	Correlation between age and weight centiles	24
5.	Distribution of weight as per gender	26
6.	correlation between age group and height centile	27
7.	Distribution of height and gender	28
8.	percentage of different grades of SMR	30
9.	Transfusion requirement	32
10.	Distribution of iron overloading rate with age	34
11.	Showing correlation between iron overload rate and mean dose of different iron chelators	34
12.	correlation between iron overloading rate and baseline serum ferritin levels	36
13.	last ferritin and iron overloading rate	37
14.	Correlation between iron overloading rate and different chelators	38
15.	Shows the percentage of patients with serum ferritin in different category	40
16.	correlation between serum ferritin (baseline) with age and gender	42
17.	correlation between serum ferritin (final) with age and gender	43

18.	correlation between serum ferritin (final) with age at enrolment	44
19.	Shows correlation between baseline serum ferritin levels and different ironchelators	45
20.	Shows correlation between last serum ferritin levels and different iron chelators	46
21.	cardiac MRI T2*	47
22.	Change in number of patients as per cardiac MRI T2*	48
23.	correlation between age and cardiac MRI T2*	49
24.	correlation between Cardiac MRI T2 * and iron chelators	50
25.	Average liver iron concentration trend over years	52
26.	Change in number of patients as per liver iron concentration	53
27.	correlation between LIC and iron chelators	54
28.	Distribution of drugs	56
29.	Showing mean dose of deferasirox as a single and in combination	58
30.	: Mean doses of deferasiro	58
31.	Shows the correlation between compliance and different iron chelators for 146 patients	63

LIST OF FIGURES

Fig. No.	Title	Page No.
1.	Pathogenesis of thalassemia	6
2.	Phenotypic features of thalassemia patients	7
3.	Cardiac iron overload and management	16
4.	Distribution of patients as per their enrolment year	19
5.	Age wise distribution	20
6.	Gender wise distribution	20
7.	Shows the mean age at diagnosis, at enrolment, and the start of chelation	21
8.	Geographical distribution	21
9.	SOCIOECONOMIC SCALE	22
10.	Distribution according to blood groups	22
11.	Weight distribution as per IAP centiles	25
12.	weight percentile and gender	26
13.	Height centile and age group	27
14.	Distribution of height percentile as per gender	28
15.	BMI distribution	29
16.	SEXUAL MATURITY RATE (TANNER'S STAGING)	30
17.	Distribution of average hemoglobin	31
18.	Average haemoglobin trend over the years (2007 - 2022)	31
19.	Showing annual transfusion requirement trend	32

20.	Serum ferritin trend over 15 years	39
21.	Shows serum ferritin categories (baseline and last follow-up)	40
22.	Cardiac MRI T2* trend over nine years	47
23.	Trend and Distribution of cardiac MRI T2* values over the years	51
24.	Liver MRI trend over years	52
25.	Trend of changing LIC over the years	55
26.	Mean dose of iron chelators	57
27.	Months of exposure with standard duration for iron chelators	57
28.	Shows different clinical adverse effects	59
29.	Laboratory parameters of adverse effects	60
30.	Shows different drugs causing different adverse effects	61
31.	COMPLIANCE	62

BABA FARID UNIVERSITY OF HEALTH SCIENCES
Sadiq Road, Faridkot-151203 (Pb.) INDIA
Phone No. 91-1639-256253 and Fax No. 91-1639-256234
Website: www.bfuhs.ac.in, Email: bfuhspc@gmail.com
(BFUHS – UNIVERSITY LIBRARY- Coordinator APC)

11-BFUHS (LI-PC-134)24/817 Dated: July 12, 2024

Plagiarism Verification Certificate

Title of the thesis: **An Observational Study Of Iron Chelation Practices in Thalassemia Day Care Center Of A Tertiary Care Hospital In Punjab.**

Total Page: **76 (Seventy-Six only) eFSPC (eFile Sent for Plagiarism Check)**

Researcher: **Veronica Banal**

Supervisor: **Dr. Shruti Kakkar**

Co-Supervisor: **Dr. Deepak Bhat and Dr. Sandeep Kaushal**

Research Centre: **Dayanand Medical College and Hospital, Ludhiana**

This is to report that the above thesis was scanned for similarity detection. Process and outcome is given below:

DID:	**2106478**	Software used:	**DRILLBIT**
Date:	**July 12, 2024**	Similarity Index:	**9% (Below 10 Percent)**

Total words count: **12595 (eFSPC)**

The complete report is submitted for review by the Supervisor and Co-Supervisor.

University Coordinator/
Name & Signature (Checked by)
(From University library)

The complete report of the above thesis has been reviewed by the undersigned. (Check Box)

☐ The similarity index is below accepted norms.

☐ The similarity index is above accepted norms, because of the following reasons:

1.....
2.....
3…….....
4…….....
5……

The thesis may be considered for the award of degree. (Relevant documents attached).

Research Scholar **Co-Supervisor** **Supervisor**

INTRODUCTION

Thalassemia is the most common single-gene disorder worldwide genetic hereditary condition. It is an autosomal recessive disease characterized by impaired synthesis of polypeptide chains of normal hemoglobin leading to anemia.[1] Based on the clinical severity and transfusion requirement, thalassemia syndromes can be phenotypically categorized into Transfusion-dependent thalassemia (TDT) and Non-transfusion-dependent thalassemia (NTDT).

Patients with transfusion-dependent β-thalassemia usually develop severe life-threatening anemia, hepatosplenomegaly, growth retardation, jaundice, and bony changes within the first few years of life.[2] Chronic blood transfusions are required for the alleviation ofanemia and related symptoms. However, regular red blood cell transfusions result in iron deposition in various organs and tissues, primarily the liver, heart, and endocrine glands.[3] Ultimately, the tissue damage occurs leading to organ dysfunction and failure. Therefore, iron overload causes significant morbidity and mortality in patients with transfusion-dependent β-thalassemia.

Iron is one of the essential elements in the body which needs to be firmly regulated. Iron overload occurs in multiple vital organs after regular transfusions along with rising serum ferritin value, usually over 1000 µg/L.[4] The iron excess is initially stored in the RAS which has a capacity of about 10–15 g, and then in all parenchyma, resulting in free radical production which can cause serious side effects such as chronic fatigue, mental retardation, delayed sexual maturity, impotence and infertility, cardiac dysfunction (arrhythmia, cardiomyopathy), liver cirrhosis, liver cancer and hepatitis,and metabolism dysfunction (diabetes, hypogonadism, thyroid disorders, parathyroid and less level of adrenal glands.[5] The others include skin color changes, abdominal pain, splenomegaly, arthritis, depression, hair loss, infection with HIV, HCV and HIV, venous thrombosis, and osteoporosis.[6] A study was conducted in Italy, and the survival probability at 30 years of age was

83.6%. It was found that in males having serum ferritin >1000ng/ml, the independent risk factor for death was heart disease.[6] In another cohort study of patients of median age 23.2 years, 93 deaths were observed out of a total of 709 beta-thalassemia patients. The most common cause was found to be heart disease. In a study from South India, in a cohort of 1087 patients 41 deaths were recorded. It was observed that 51.6% of deaths occurred due to infections and 35.4% occurred from severe organ iron overload. The iron overload increased with age.[7]

Over the years, there has been significant advancement in regular transfusion therapy and iron chelation therapy which has improved the quality of life of patients with TDT.[8] ICT has transformed thalassemia from a rapidly fatal disease to a compatible disease with good survival rates. The life expectancy of patients with thalassemia depends on compliance with medical treatment.Most patients in India are on generic deferasirox.

Iron chelators are pharmacological drugs that are designed to bind and remove excess iron from the body. [9] The iron chelators interact with low molecular labile iron pools rapidly and help in decreasing the iron molecules in the bloodstream. The development of orally effective iron chelators such as deferiprone and deferasirox is intended to improve compliance.[10] Combined chelation treatment is emerging as a potential alternative to monotherapy. Combining a weak chelator that has a better ability to penetrate cells with a stronger chelator that is more efficient in urinary excretion and penetrates poorly in cells may result in improved therapeutic effects through iron shuttling between the two compounds.[11] The efficacy of combined chelation treatment is additive and increases the success rate in patients previously failing deferasirox or deferipronemonotherapy. The aim of iron chelation therapy is primarily to prevent the accumulation of excess iron, hence decreasing iron overload and its complications such as hepatic, endocrinological, and cardiac dysfunction.[12] Effective chelation therapy limits treatment-related complications and improves the overall

survival of thalassaemic patients. Compliance and difficulties with precise monitoring of response, however remain a major issue. A study on long term efficacy and safety in Taiwanese children had enrolled 60 patients. [13] The lifelong duration, the presence of adverse events, and the frequency of administration of the available chelating agents are responsible for non-compliance or suboptimal compliance. The following are the three drugs being used most commonly used:

Deferoxamine: This drug was discovered in and remains the gold standard for iron chelation. Compliance with deferoxamine has been low due to need for parenteral infusion, narrow safety margin and higher cost.[14]

Deferiprone: It is the first oral iron chelator which has been widely used in India. It was approved in 1995 and has been used ever since. It has a short half-life and needs to be administered 3-4 times a day.[15]

Deferasirox: This drug was launched in 2009 in India and has become the most commonly used iron chelator due to oral and once daily administration and preferred safety profile of the drug.[16] In a randomised control trail with deferasirox vs deferoxamine, it was found that the both groups had shown fall in serum ferritin and lowered the liver iron concentration. The most common adverse effect seen was GI disturbance and rash.

In another Indian study a cohort of 50 patients was studied and all of the patients were on deferasirox. The mean serum ferritin was found to be 4354 ng/ml and 36% had ferritin > 5000ng/ml. Further 70% patients needed higher doses >30 mg/kg/day. There was a fall in serum ferritin in 56 % patients in 3 months, six patients had serum ferritin <1000 ng/ml. The most common adverse effect was rise in serum creatinine (11%) followed by GI disturbance (10%) and rash in 8 % patients.

The table below shows the different properties of different iron chelators:

Table 1: Iron chelators and their properties

PROPERTY	DEFERASIROX	DEFERIPRONE	DEFEROXAMINE
ROUTE	oral	Oral	intravenous/ subcutaneous
DOSE	20-30 mg/kg/day	75mg/kg/day	25-50 mg/kg/day
SIDE EFFECTS	GI disturbance, Rise in creatinine	GI disturbance, agranulocytosis/ neutropenia Arthralgia	Rash Auditory and visual defects

The above drugs are used as monotherapy or in combination. Overall, the combination therapy is well tolerated. However, there are many side effects, so the efficacy is measured against the adverse effects via different measurable parameters like serum ferritin, liver iron concentration, and cardiac iron overload.[17] The measures for the safety of the iron chelators are elevated transaminases and sexual maturity rate. In developing nations like India, poor availability of proper medical care, safe and adequate red blood cell transfusions together with high cost and poor compliance with chelation therapy are the major obstacles. Not many studies have been done to compare the safety and efficacy of individual drugs and in combination. So, this observational study is done to add significant evidence and comparison of the safety and efficacy of iron chelation therapy.

AIMS AND OBJECTIVE

1. To study the iron chelation practices in the thalassemia day care center of a tertiary care hospital in Punjab.
2. To compare the outcomes in terms of iron overload across various treatment regimes.

REVIEW OF LITERATURE

Thalassemia is an inherited blood disorder caused by abnormal hemoglobin. Depending upon the type of thalassemia symptoms can vary from mild to severe.[18] The basic defect in beta-thalassemia is a reduced or absent production of beta-globin chains with relatively excess alpha chains. These chains form tetramers, accumulate, and then precipitate in the erythroid precursors, which ultimately causes oxidative membrane damage to the cells.[19] Ultimately ineffective erythropoiesis takes over resulting in severe anemia. On the other hand, there are excess beta globin chains which are unpaired and are unstable. These beta globin chains also precipitate and cause oxidative damage.

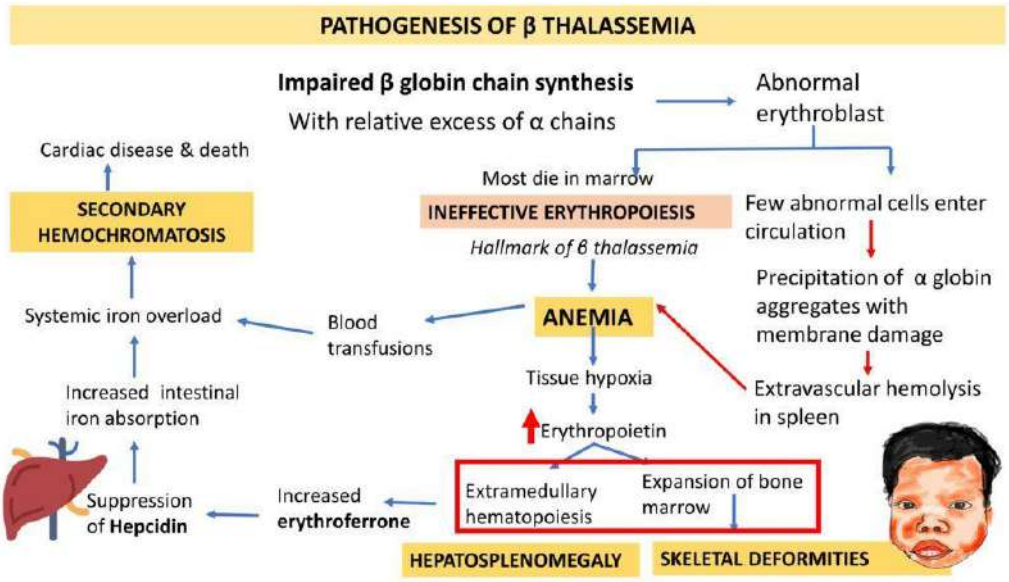

Figure 1: Pathogenesis of thalassemia

SYMPTOMS: may vary according to type and severity of anemia

During mild to moderate anemia:[20]

- Tiredness
- Weakness
- Breathlessness
- Tachycardia
- Pallor

Dizziness

Lightheadedness

Muscle cramps

Children with severe types of thalassemia may have:

Jaundice

Hepatosplenomegaly

Dark urine

Loss of appetite

Developmental delay and abnormalities

Changes in facial features

In mild cases, symptoms may not be apparent until later in childhood or adulthood.

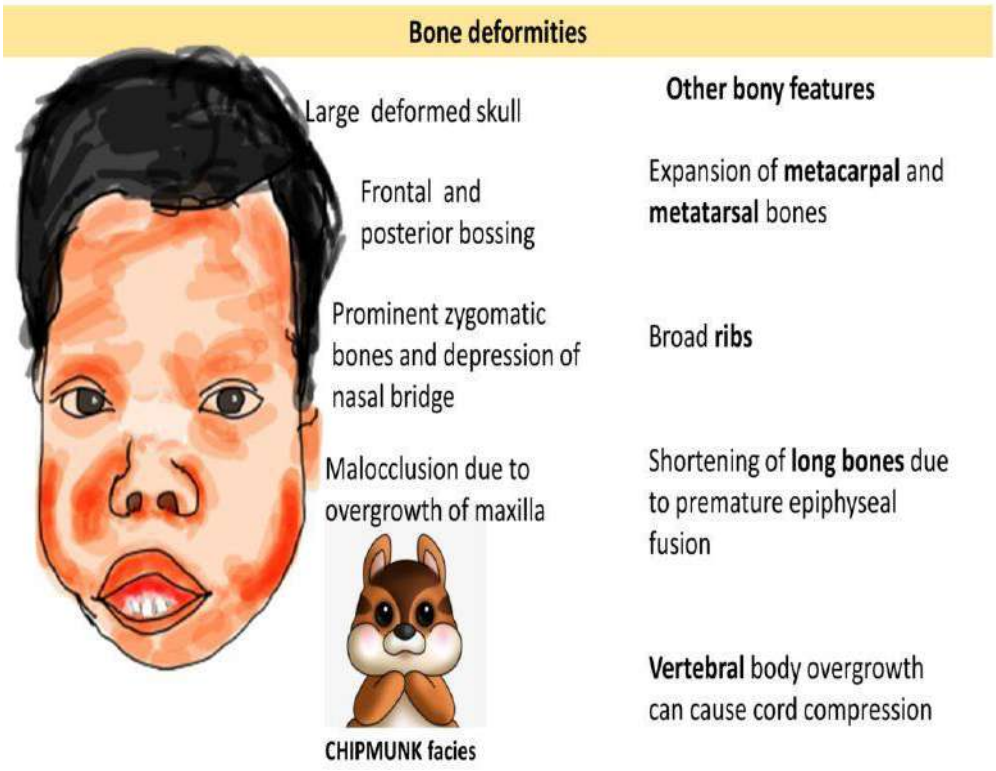
Bone deformities
Large deformed skull
Frontal and posterior bossing
Prominent zygomatic bones and depression of nasal bridge
Malocclusion due to overgrowth of maxilla
CHIPMUNK facies
Other bony features
Expansion of metacarpal and metatarsal bones
Broad ribs
Shortening of long bones due to premature epiphyseal fusion
Vertebral body overgrowth can cause cord compression

Figure 2: Phenotypic features of thalassemia patients.

HEMOSIDEROSIS:

In severe cases, multiple blood transfusions are required for survival. [21] However, iron overload (Hemosiderosis) is an inevitable complication found in patients, which may bedue to ineffective erythropoiesis, increased gastrointestinal absorption, lack of a physiologic mechanism for excreting excess iron, and above all multiple blood transfusions.[22] 200-250 mg of elemental iron is present in each transfused unit of packed red blood cells.[23] Transfusion iron normally amounts to 0.2 to 0.6 mg/kg per day for TDT patients, with an estimated monthly average transfusion volume of red blood cells filled with 2 to 4 units. As the human body has no effective mechanism to remove excess iron load caused by blood transfusion, this excess iron accounts for the disruption of major vital organs' functioning and causes irreversible damage.

IRON OVERLOAD MANAGEMENT:

The primary goal of chelation therapy is to maintain safe levels of body iron at all times, by balancing iron intake from blood transfusion with iron excretion by chelation (iron balance).The availability of oral iron chelators in recent years has enabled clinicians to serve to the needs of these patients. Possible regimens are monotherapy with either deferiprone or dual chelator whereby both drugs can be given in a combination regimen or on different days.

Review of related literature:

Cappellini et al *(2006)*[23] conducted a study on iron chelation with deferasirox in children for a 5 year follow-up and studied the long-term efficacy and safety of deferasirox in patients aged >2 years. This study concluded that the long-term treatment with deferasiroxfor <5 years is generally well tolerated and effectively reduces the iron burden.

Glickstein et al(2006)[24] conducted a study on the action of chelators and myocardial cells saturated with iron. This study compared all three iron chelators and concluded that they acted as scavengers for

unbound and labile iron molecules in plasma and cardiac cells. The deferoxamine acts primarily by eliminating LPI. The oral chelators deferasirox and deferiprone are rapidly absorbable in the intracellular labile iron compartments which makes them potent and efficacious for protection. This further reduces the cardiac damage induced by iron overload and possibly damage reversal.

Cohen et al (2008) [25] conducted a study onsplenectomized patients to see the effect of transfusional iron intake and their response to chelation therapy in thalassemia major. This study concluded that patients who underwent splenectomy had lower transfusional iron intake and further had a higher reduction in iron stores as compared to the patients with intact spleens. It was further emphasized to monitor the Transfusional iron intake regularly and monitoring the transfusional iron loading rate should be done while deciding the appropriate dose of an iron chelating agent.

Berdoukas et al (2010) [26] conducted a study to find optimal iron chelation therapy for patients with thalassemia major. It was observed that the combination of deferoxamine and deferiprone was the best combination to achieve normal serum ferritin. Starting the chelation in a younger age can prevent short stature and help in sexual maturation along with other iron-related morbidities. To achieve this compliance and consistency is required. Adherence to the treatment is now likely the primary barrier to longevity.

Cappellini et al (2011)[27] conducted a study on iron chelation with deferasirox in adult and pediatric patients with thalassemia major: efficacy and safety during 5-year follow-ups. To evaluate the long-term efficacy and safety of once-daily oral iron chelation with deferasirox, patients aged > 2 years who completed a 1-year, phase 3, randomized trial entered a 4-year extension study, either continuing on deferasirox (deferasirox cohort) or switching from deferoxamine to deferasirox (crossover cohort).This prospective study suggested that the treatment

for < 5 years is generally well tolerated and effectively reduces iron burden.

Pepe et al (2011) [28] conducted a study on ICT in thalassemia major patients. Cardiac iron and function comparison was determined by quantitative magnetic resonance imaging. Myocardial iron concentrations were measured by the T2* and ventricular function were evaluated. Liver iron concentrations were measured by the T2* multi-echo technique. It was found that the global heart T2* value was higher in the deferiprone (34±11ms) than in the deferasirox (21±12 ms) and the deferoxamine groups (27±11 ms). p-value was significant. (*P*=0.0001). The cohort of patients treated with oral deferiprone showed less myocardial iron burden and better global systolic ventricular function compared to the patients treated with oral deferasirox or subcutaneous deferoxamine.

Hoffbrand et al (2012) [29] conducted a study which mainly focused on the use of MRI to determine iron chelation therapy and to monitor theprogress. All the iron chelators were studied for their efficacy and safety. This study lay emphasis to when to initiate, switch or increase the dose of the drug. The combination of all the drugs could improve the overall quality of life of patient.

Al-Moshary et al in 2020 [30] studied liver function tests of patients with TDT. The LFTs and serum ferritin levels were correlated in these patients and it was found that iron deposition is the main reason for transaminitis. There is a definitive correlation between serum ferritin, ALT/AST and ALP while not much correlation was found between serum ferritin and bilirubin.

The study by Sidhu et al 2021[31] aimed to assess adherence to iron chelation in patients with TDT. It aimed to evaluate the various causes of non-adherence and also to study the impact of non-compliance and non-adherence on the related complications with iron overload. With a

mean age of 15.07+7.68 years, it was observed that in 10.7% of patients were non-adherent. Serum ferritin levels were significantly higher in the non-adherent group (3129.8+1573.2 µg/l) than in the adherent population (2013.1+1277.1 µg/l). Also, cardiac and liver iron overload was comparatively high in the non-adherent population. The most common reasons for non-adherence were difficulties in drug administration and the quantity of medicines to be taken regularly. It was concluded that nearly 11% of patients with transfusion-dependent thalassemia were non-adherent resulting in higher iron overload.

Another study conducted by Parakh et al in 2022 [32] studied the correlation of MRI T2* and serum ferritin levels in children with TDT. The time interval between fibro scan and MRI T2* kept was 60 days. Liver iron overload was calculated based on MRI T2* values and was found in 96.6% of the patients. Based on the MRI analysis, patients were divided into three categories as: 13.6% of patients had mild, 17% had moderate, and 66% of patients had severe iron load respectively. The study showed a significant correlation between transient elastography and MRI T2*.

A study by Mohamed et al was carried out in 2022 [33] amongst children in the age group of 6-18 years aiming at non-invasive assessment of liver enzymes and risk factors of liver fibrosis using transient elastography. The study concluded that 52.8% of the patients had severe fibrosis and 9.4% of the people had HCV serology-positive results. Significant liver fibrosis was correlated with serum ferritin levels, HCV infection, age, blood transfusion frequency, and irregular chelation therapy. However, no significant correlation was noted with sex or BMI.

Helen S. Maurer, MD et al(1988) [34] conducted A prospective study of ICT in sixteen patients aged between 3 to 17 years with transfusion-dependent β-thalassemia major. In the beginning at the onset of chelation therapy with deferoxamine, a liver biopsy specimen was

obtained from each patient at the start of the study, and thereafter. Liver histologic features, iron content, and iron excretion were assessed during the study. Hepatic iron levels from liver biopsy specimens were correlated with serum ferritin levels. It was found that in the younger patients, the liver was found to be less heavily iron-loaded. It appeared that in patients with higher serum ferritin levels, hepatic iron appeared to have reached a certain saturation level. Out of all sixteen patients, fourteen had already developed fibrosis of the liver in their initial biopsy specimens. Subsequent biopsy specimens from nearly all of the patients showed a remarkable reduction in iron concentration, but only two of seven patients showed improvement in the degree of hepatic fibrosis three to five years later. Patients less than 8 years old had a normal pattern of linear growth until approximately the age of 10 years, and following there was seen a rapid decrease to the 30th to 40th percentile. Two patients, aged 18 and 22 years, died of cardiac disease during the study. These findings suggest that chelation therapy in patients with transfusion-dependent thalassemia needs to be initiated at an early age, preferably before 3 years, if significant liver fibrosis and growth impairment are to be effectively prevented.

Sarmi Patel et al 2012 [35] conducted a study on 53 thalassemic of the prevalence of thalassemia and its correlation with liver function tests in different age and sex groups in the Chittagong district of Bangladesh. The study was conducted on patients, and the relationship between the patients' ages and sex was made. The cases are taken based on their age (2-30 years), Among them were 21 (39.6%) female and 32 (60.4%) male with clinical jaundice with a history of chronic blood transfusion. Patients who had jaundice due to viral hepatitis,due to arsenic poisoning and splenectomised were excluded and so were those with. Liver function tests were evaluated. With an average of 15.1% (8 in no.) beta-thalassemia, 7.5% (4 in no.) beta-thalassemia major, and 77.4% (41 in no.) E-beta-thalassemia cases have been found in the study. Mean (±SD) TSB in a total of 53 subjects with age

groups 2-10 years and 21-30 years is significant. The study concluded that in thalassemic patients more the age, the more the disease progresses with their complications. Hepatic complications are mainly due to being hepatocellular rather than obstructive.

G M Brittenham, P M Griffith, et al 1994 [36] conducted a study on the Efficacy of deferoxamine in preventing complications of iron overload in patients with thalassemia major patients. In this study,59 patients (30 were female and 29 male; an age range, of 7 to 31 years were evaluated periodically for 4 to 10 years or until death. At the follow-up visit, a detailed clinical and laboratory evaluation was done. Hepatic iron stores were measured with a noninvasive magnetic device. The iron burden was assessed by magnetic measurement of hepatic iron stores. Each increase of one unit in the ratio of transfusional iron load to deferoxamine use was associated with an increased risk of impaired glucose tolerance, and diabetes mellitus. Hence, concluded the early use of deferoxamine in an amount proportional to the transfusional iron load reduces the body iron burden and helps protect against diabetes mellitus, cardiac disease, and early death in patients with thalassemia major.

S Daar, A V Pathare, et al [37] conducted a clinical trial on 91 thalassemia patients aged between 2-30 years who were on combined therapy of deferoxamine and deferiprone and receiving regular transfusional support. All received packed red cells every 3-4 weeks to maintain pretransfusion hemoglobin concentration above 9 g/dl. All had been receiving DFX at a daily dose of 40 mg kgby s/c infusion 4-5 nights /week for several years. It was noticed that despite all the chelation the patients still had developed considerable transfusional iron overload, these patients were allocated to prospectively receive additional therapy with oral iron chelator at 75 mg/kg/day body weight and continued to receive treatment with DFX. The most common adverse effects seen were severe gastrointestinal (GI) upset in six patients, two had agranulocytosis, two had arthropathy, one raised liver

enzymes, two died owing to sepsis, and two received allogeneic bone marrow transplantation. Amongst the remaining 76 patients, 21 were found non-compliant. Thus, the 55 remaining patients in the study at the end showed significant improvement in the myocardial function as assessed by the ejection fraction ($p<0.004$) and fractional shortening ($p<0.05$). Hence, the study emphasizes that beta thalassemia major patients with transfusional iron overload can be successfully treated with a combination of DFX which could lead to a progressive fall in the mean serum ferritin. Also, significant improvement was demonstrated in the echocardiographic parameters of myocardial function in patients receiving combination therapy.

Hsiu-Hao Chang1 & Meng-Yao Lu et al (2015) [13] conducted a study on the tolerability and efficacy of deferasirox on children. Out of 49 patients in the cohort, 42were continued in the study for analysis of efficacy. The mean serum ferritin levels of these patients decreased significantly from 4279 ng/mL at the start of deferasirox treatment (baseline) to 1713 ng/mL after 7 years of deferasirox treatment. The common adverse effects included skin rashes (n=29, 48.3%), abdominal pain (n=23, 38.3%) and diarrhea (n=16, 26.7%). GI adverse events related to deferasirox were reported in 29 (48.3%) patients. Most of these drug-related adverse events were mild to moderate in severity, manageable, and happened in the first 2 years of deferasirox treatment.

Wan Jin Lee, Nurul Ain MohdTahir et al (2024) [38] conducted a study to draw the relation between compliance and health outcomes of thalassemia patients. It was found that the compliance ranges from 20.93 to 75.3%. The majority of studies demonstrated a negative correlation between compliance and serum ferritin, while numerous studies revealed poor ICT compliance linked with increased risk of liver disease, cardiac disease, endocrinologic and morbidity. Inadequate compliance with ICT therapy is common. Higher compliance is correlated with lower serum ferritin and a lower risk of complications.

MATERIALS AND METHODS

An observational study was conducted in the Thalassemia Day Care Centre in the Department of Paediatrics, Dayanand Medical College and Hospital, Ludhiana from July 2022 to December 2023 after obtaining approval from the Institutional Ethics Committee.

SETTING: All the patients with Transfusion-Dependent Thalassemia registered with the centre and receive leuco-depleted PRBC 15-20 ml/kg every 3-5 weeks to maintain a pretransfusion Hb between 9-10.5 g/dl. Patients are started on iron chelation therapy after 10 transfusions or when serum ferritin > 1000ng/dl. Patients /Parents are counseled regarding all three ironchelators (Deferoxamine**,** Deferiprone, and Deferasirox) available. The benefits, adverse effects, monitoring, and expected cost of each of them are explained and chelation is started with the drug chosen by the family provided there was no contraindication. Serum ferritin is monitored every 3-6 months once the Iron chelation therapy is initiated.

The following parameters are monitored for assessing the safety and efficacy of iron chelation therapy

Table 2: Investigation and frequency

	WHEN TO COMMENCE	**FREQUENCY**
SERUM FERRITIN	After 10 transfusions	3 monthly
MRI	After 10 years of age	Annually
CARDIAC T2* >20ms 10-20ms <10ms		 2 yearly Annually 6 monthly
LIC 1.8 -7mg/g dry wt >7- <15mg/g dry wt >15mg/g dry wt		 1-2 yearly Annually 6-12 monthly

Table 3: Lab investigation and frequency

Toxicity of Chelators	Frequency
AST/ALT, Creatinine	Monthly
Complete blood count	Monthly
Opthalmology evaluation	Annually
Hearing Evaluation	Annually

Modification in iron chelation therapy is done based on results of serum ferritin and MRI T2* as follows:

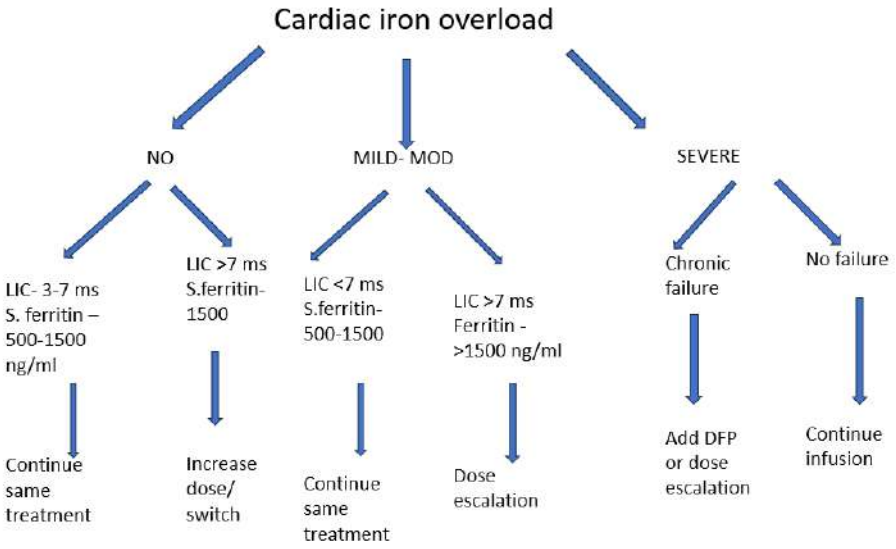

Figure 3: cardiac iron overload and management

SOURCE OF DATA: All children (1-18 years) with TDT receiving ICT and on regular follow-up in theTDCC in the Department of Pediatrics, Dayanand Medical College and Hospital, Ludhiana were included in the study.

INCLUSION CRITERIA:

1. Patients with transfusion-dependent thalassemia between the age group of 1 -18 years who have taken at least 1 dose of iron chelation.
2. Patients who consent to be a part of the study.

EXCLUSION CRITERIA:

1. Non-transfusion-dependent thalassemia patients.
2. Patients <1 and >18 years of age.
3. Patients who do not give consent.

Patient assessment regarding the hemoglobin and transfusion details, socioeconomic details, serum ferritin levels, liver enzymes, and serum creatinine were recorded. Any adverse effect of deferasirox was also recorded from the patient files. MRI T2* reports were included in the study. Vision and Hearing evaluation was done.Patient records were revised for diagnostic details. The levels of serum ferritin, MRI T2* etc were recorded along with any adverse reaction experienced by the patient.

PARAMETERS OF EFFICACY:

1. Serum ferritin levels repeated every 3 months.
2. Cardiac MRI T2* annually
3. Liver iron concentration (by MRI T2)
4. Growth [(weight/, height/ tanner's staging (in 10-18years)]

PARAMETERS OF SAFETY:

1. Hemogram
2. SGPT/ SGOT
3. Serum creatinine levels
4. Audiometry
5. Ophthalmologic examination

STATISTICAL ANALYSIS

Data will be described in terms of range; mean ±standard deviation (± SD), frequencies (number of cases), and relative frequencies (percentages) as appropriate. For comparing categorical data, the Chi-square ($\chi 2$) test will be performed and the Fisher exact test will be used when the expected frequency is less than 5. A probability value (p-value) less than 0.05 will be considered statistically significant. All

statistical calculations will be done using (Statistical Package for the Social Science) SPSS21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

OBSERVATIONS AND RESULTS

An observational study was conducted in the Thalassemia Day Care Centre of Department of Paediatrics, Dayanand Medical College and Hospital, Ludhiana over fifteen months. A total of 148 children between the age group of 1 to 18 years who had received at least one dose of iron chelation with any of the three available iron chelators either as a single agent or in combination were included in the study.

The number of patients started on chelation therapy each year have been depicted in below figure. The maximum patients were enrolled in year 2019.

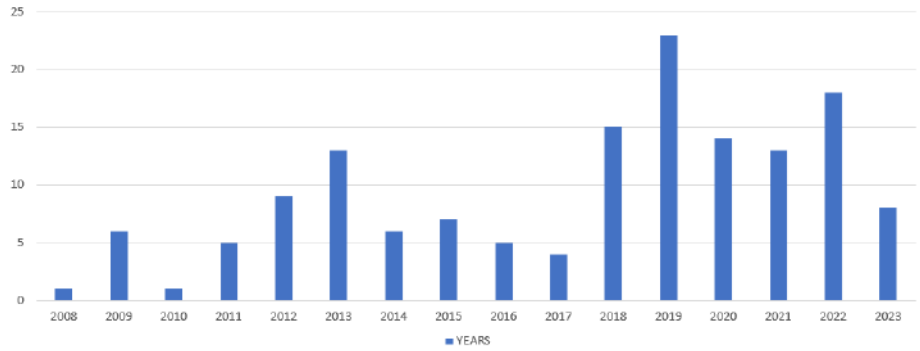

Figure 4: – Distribution of patients as per their enrolment year

A. DEMOGRAPHIC PROFILE:

The mean age of the study population was 112 ± 58.56 months (9 years 3 months) with a range of 6 months to 17.5 years. The age-wise distribution of the patients is shown in figure below. Nearly half (45.9%) of patients were > 10 years of age. Patients between 5-10 and <5 years constituted 31.1% and 23% of the study population respectively.

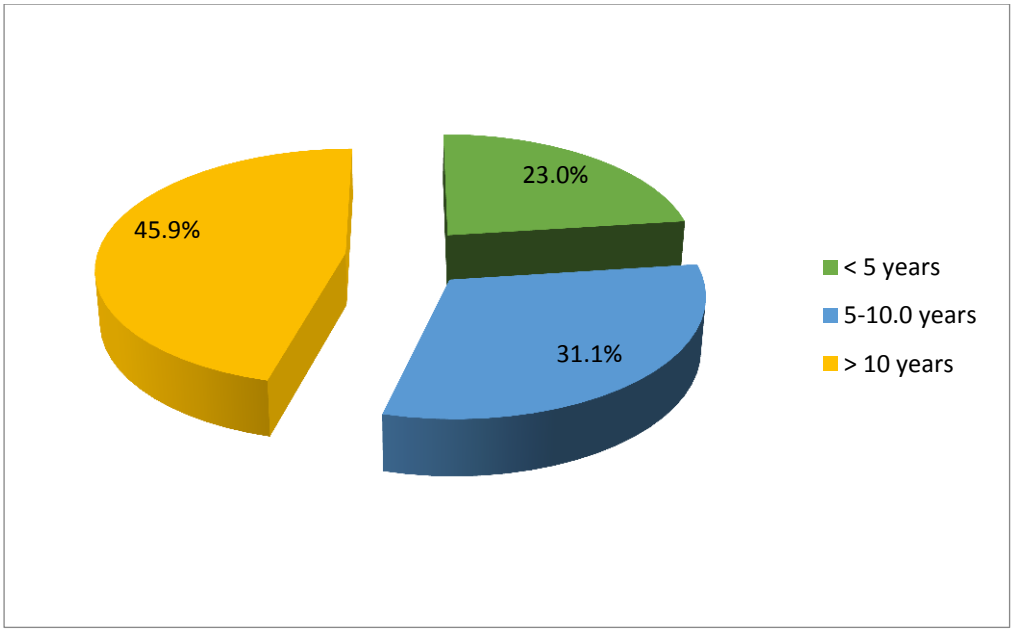

Figure 5: Age wise distribution

The male-to-female ratio of the study population was 1.84:1.

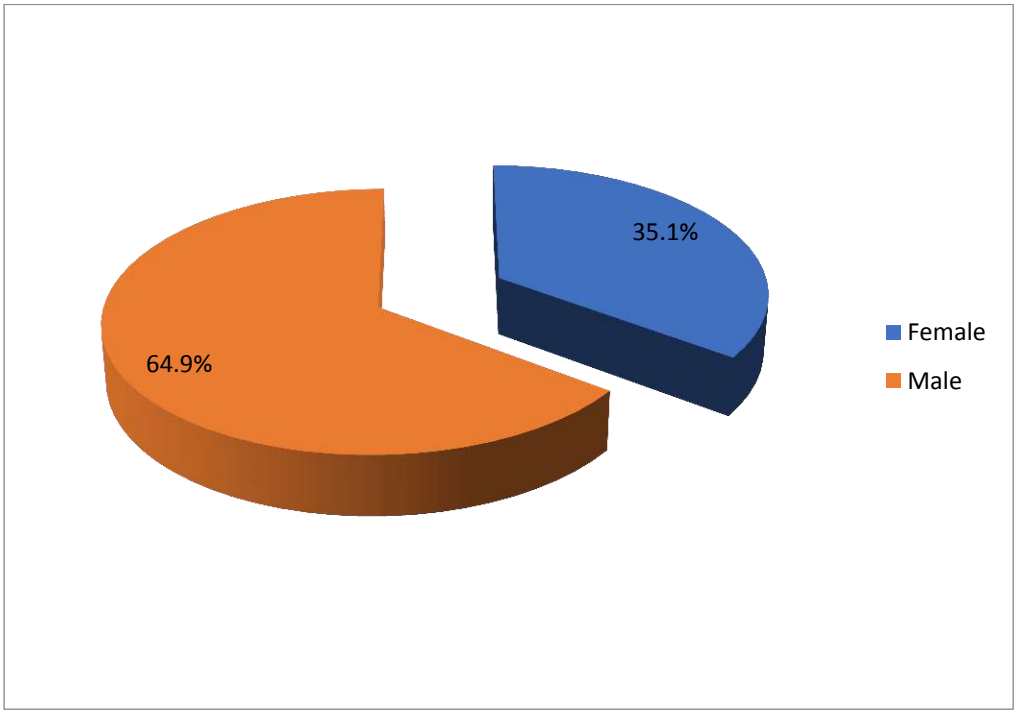

Figure 6: Gender wise distribution

The mean age at diagnosis of TDT was 8.19 ± 3.8 months (Range 2.9 months- 2 years) and the mean age of enrolment at TDCC was 41.9 ± 42.8 months (Range – 3months – 17 years). The average age at starting iron chelation was 58.06 ± 40.23 months (Range – 10 months - 17 years).

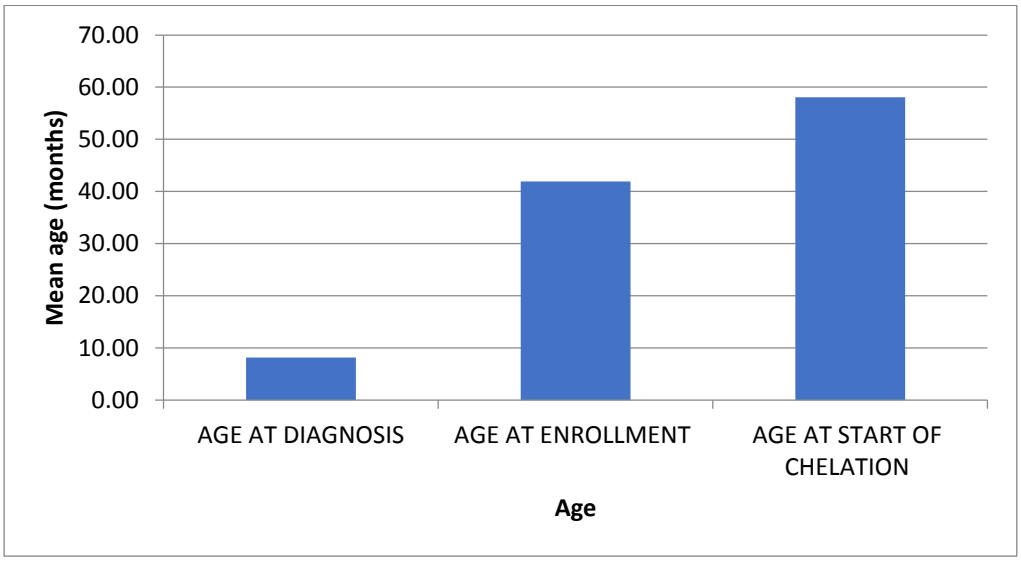

Figure 7: Shows the mean age at diagnosis, at enrolment, and the start of chelation

One hundred and nine (73.6%) study participants resided in an urban area whereas 26.4% (n=39 patients) were rural dwellers.

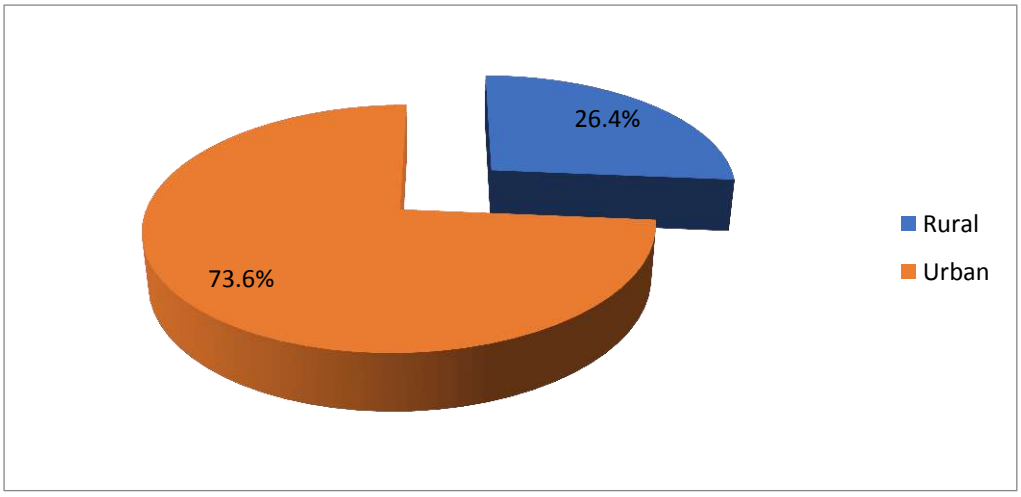

Figure-8 : Geographical distribution

The socioeconomic status was assessed using the Modified Kuppuswamy socioeconomic scale: 2022 update. Most patients (35.8%) belong to the lower middle class followed by the upper middle class accounting for 33.1%.

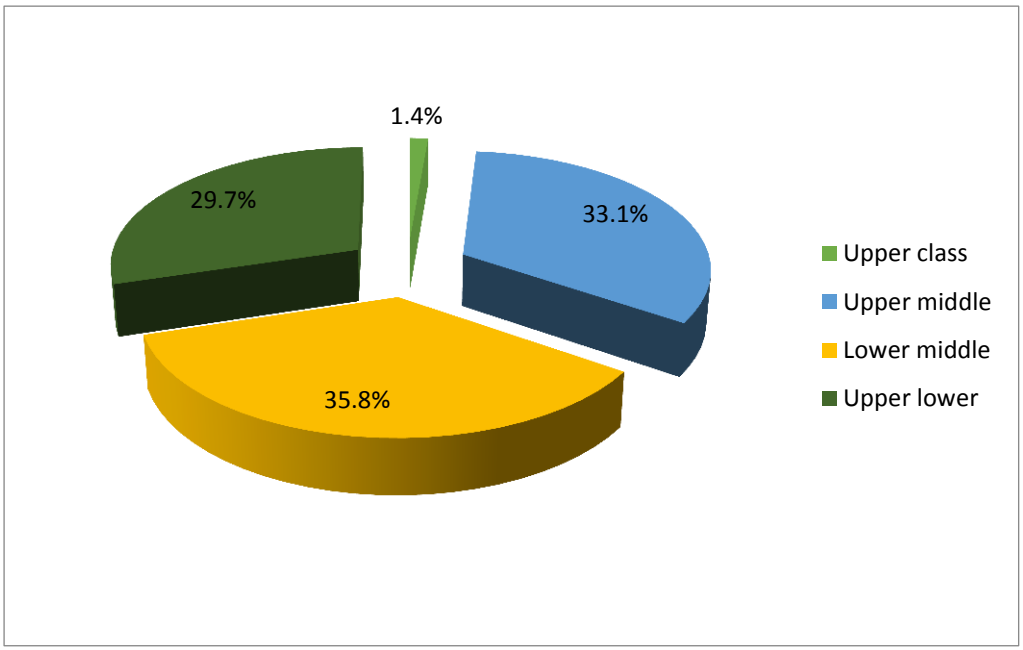

Figure 9: SOCIOECONOMIC SCALE

The distribution of the patients as per their blood groups is shown in the graph below. B positive was the commonest blood group (35.1%) and A- and AB- were the least common blood groups (0.7% in each group).

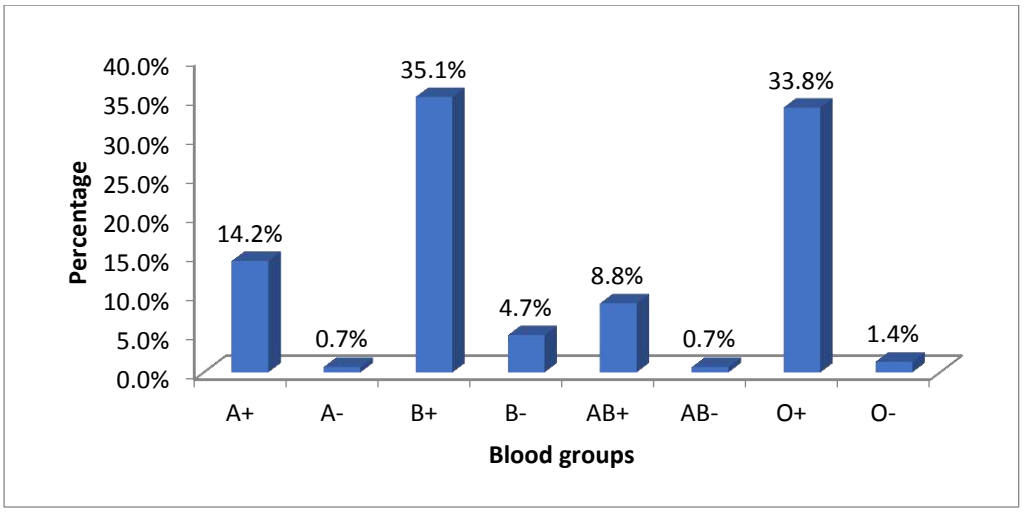

Figure 10: Distribution according to blood groups

B. ANTHROPOMETRY:

The weight, height, body mass index, and sexual development were assessed at the time of enrolment. The weight, height and BMI were interpreted as per the age-appropriate IAP growth charts. Sexual development was assessed using Tanner's staging of sexual development for girls and boys > 10 years of age.

As per the IAP growth chart, out 49 patients who were undernourished (<3rd centile) 12 were <5 years of age, 8 were between 5-10 and 29 were >10 years of age.

Twenty-one patients were between the 3rd -and 97th centile were < 5 years, 29 were between 5-10 years and 32 were >10 years of age. Weight was > 97th centile in 17 patients of the study participants.

Table 4: Correlation between age and weight centiles

		Age group						**Total**	**Chi-square value**	**p-value**
		< 5		5-10.0		> 10				
Weight (interpretation)	< 3	12	35.3%	8	17.4%	29	42.6%	49	11.796	0.019
	3-97.0	21	61.8%	29	63.0%	32	47.1%	82		
	> 97	1	2.9%	9	19.6%	7	10.3%	17		
Total		34	100.0%	46	100.0%	68	100.0%	148		

Maximum no. of patients had weight between 3-97th centile.

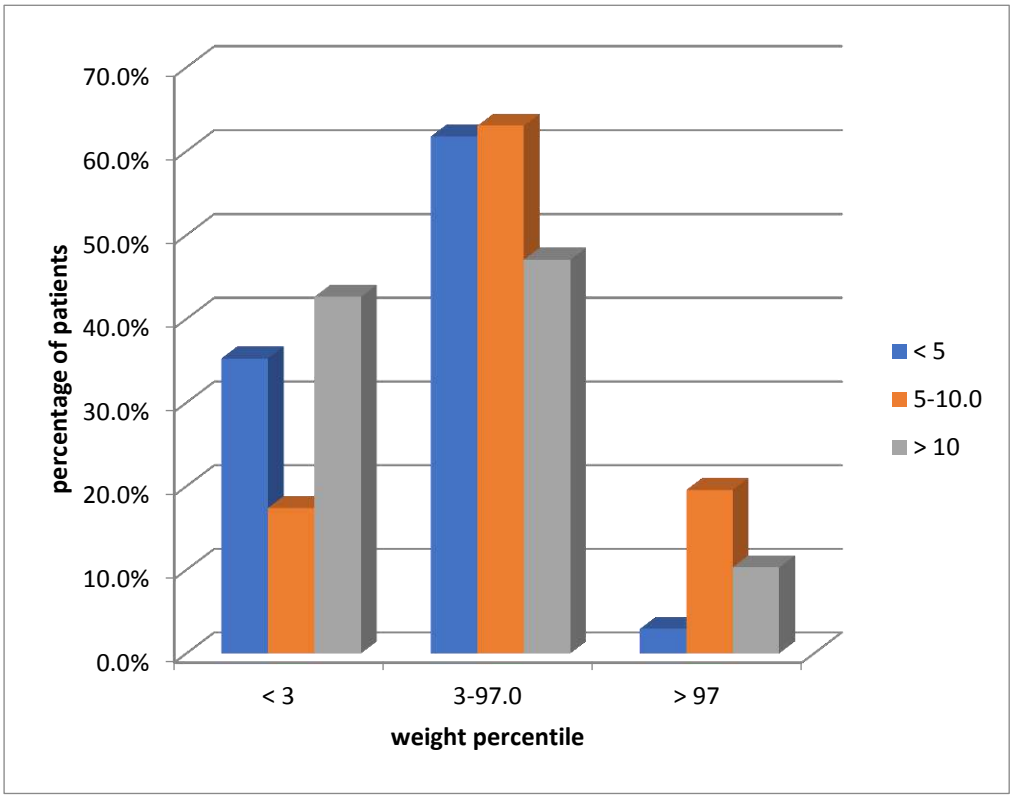

Figure - 11: Weight distribution as per IAP centiles

Out of total of 52 females maximum (n=33) weighted 3-97th centile and 49 males weighted 3-97th centile.

Table 5: Distribution of weight as per gender

		Sex				Total	Chi-square value	p-value
		F		M				
Weight (interpretation)	< 3	13	25.0%	36	37.5%	49	2.531	0.282
	3-97.0	33	63.5%	49	51.0%	82		
	> 97	6	11.5%	11	11.5%	17		
Total		52	100.0%	96	100.0%	148		

There is no significant difference in weight distribution as per gender of the patients.

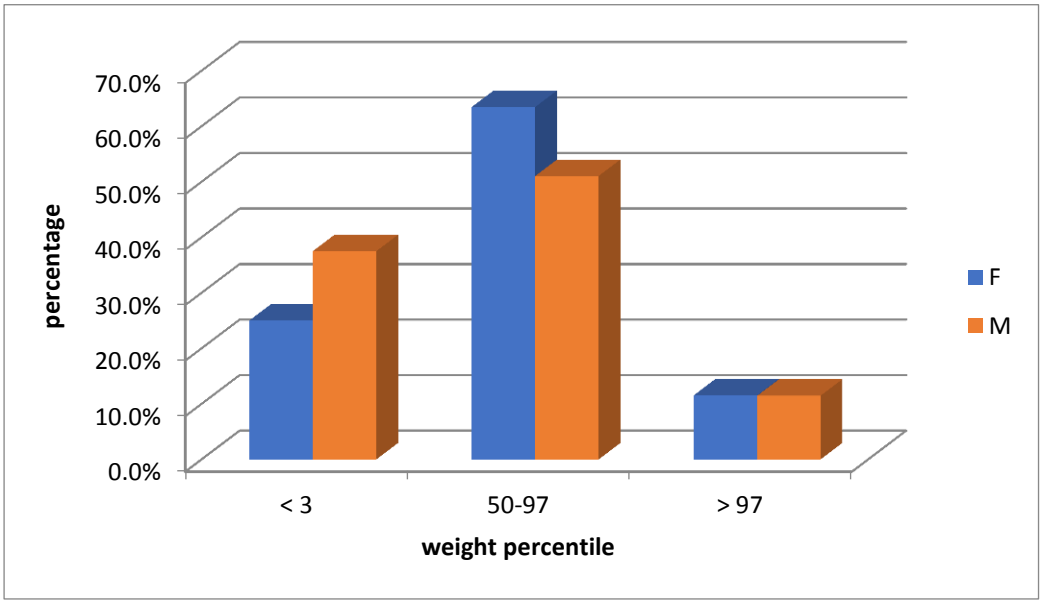

Figure 12: weight percentile and gender

As per the IAP growth charts, 40 patients were short statured (<3rd centile), and maximum proportion of patients (n=90_ were between the 50 th -and 97th centile and 18 patients were >97th centile.

Table 6: correlation between age group and height centile

		Age group						Total	Chi-square value	p-value
		< 5		**5-10.0**		**> 10**				
Height (interpretation)	< 3	7	20.6%	8	17.4%	25	36.8%	40	13.035	0.011
	3-97	22	64.7%	30	65.2%	38	55.9%	90		
	> 97	5	14.7%	8	17.4%	5	7.4%	18		
Total		34	100%	46	100%	68	100%	148		

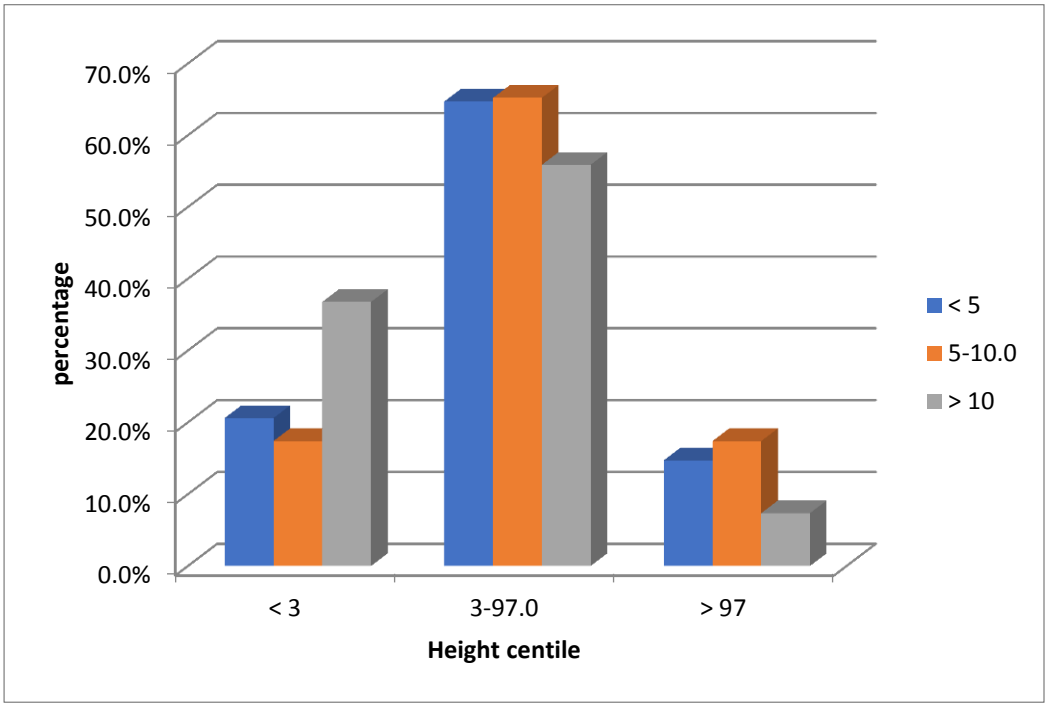

Figure 13: Height centile and age group

Out of total 52 females maximum (n=33) had weight between 3-97th centile and 57 males had weight between 3-97th centile

Table 7: Distribution of height and gender

		Sex				Total	Chi-square value	p-value
		F		M				
Height (interpretation)	< 3	14	26.9%	26	27.1%	40	0.521	0.771
	3-97	33	63.5%	57	59.4%	90		
	> 97	5	9.6%	13	13.5%	18		
Total		52	100%	96	100%	148		

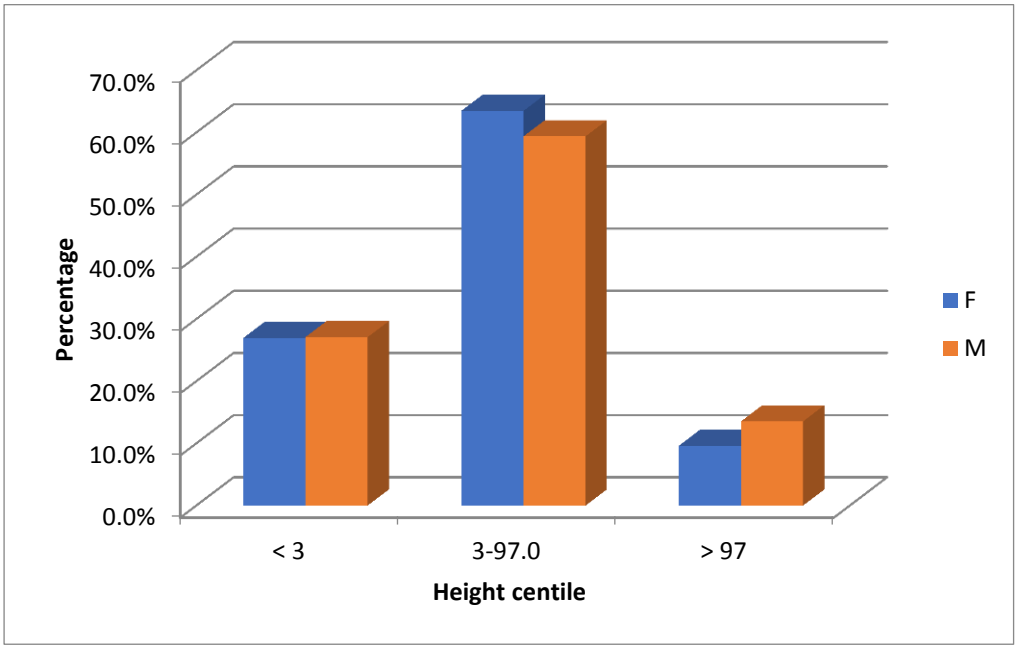

Figure 14: Distribution of height percentile as per gender

Body mass index assessment was normal in 47.3% of study participants. Overweight and obesity was present in 16.2% and 36.5 % participants respectively. None of the patients were found to be underweight

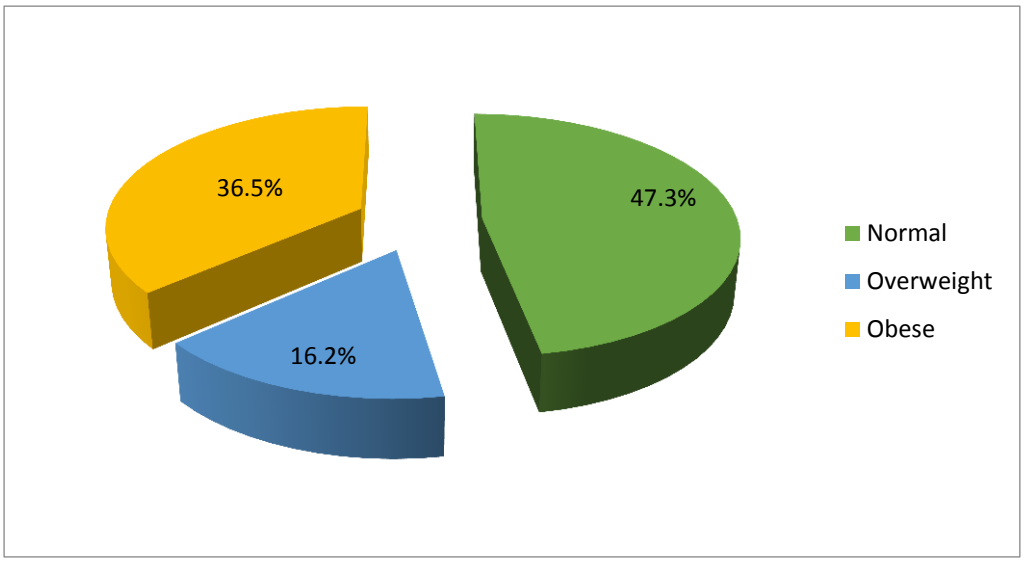

Figure 15: BMI distribution

.

Out of 148 patients, the study had 68 patients were >10 years and were assessed for SMR. Grading was done as per the following:

Grade 1: Normal progression

Grade 2: Late onset with spontaneous progression

Grade 3: Normal or Delayed onset along with pubertal arrest

Grade 4: Pubertal failure

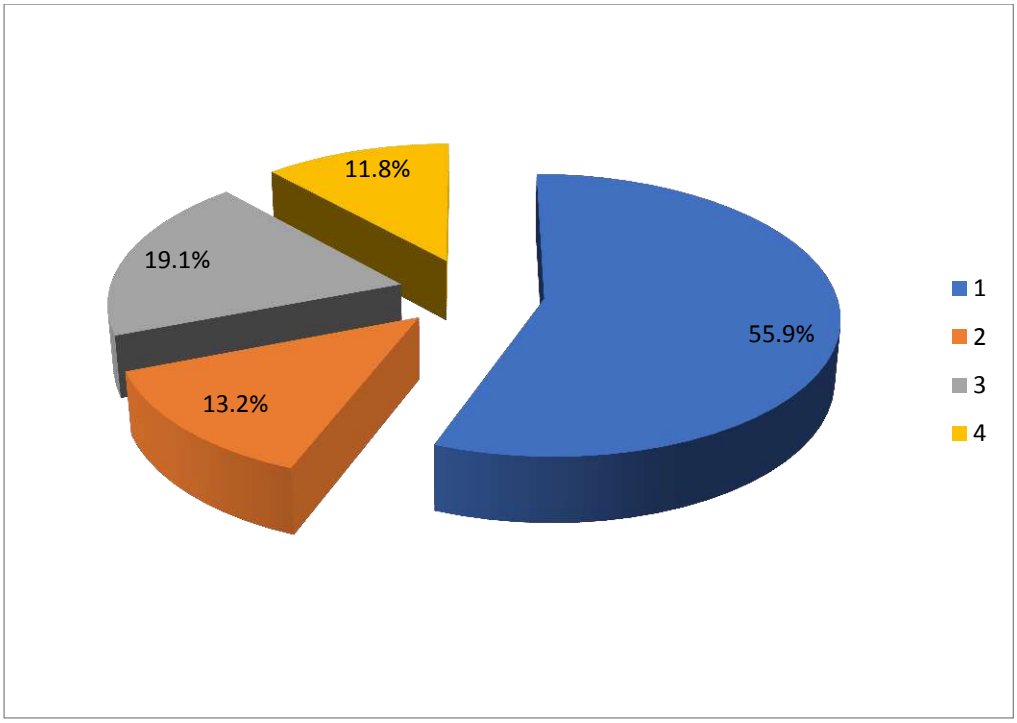

Figure-16: SEXUAL MATURITY RATE (TANNER'S STAGING)

Normal onset and progression (grade1) was seen in maximum percentage of (55.9%) patients (n= 38). Delayed puberty was seen in 9 patients (13.2%).

Pubertal arrest was seen in 13 patients (19.1%). Pubertal failure was seen in 8 patients (11.8%)

Table 8: percentage of different grades of SMR

SMR	No. of cases	Percentage (%)
1	38	55.9%
2	9	13.2%
3	13	19.1%
4	8	11.8%
Total	68	100.0%

C. TRANSFUSION DETAILS:

The average Hb at the time of enrolment was found to be 9.45 gm/dl (± 0.50) The average Hb was maintained between 9-10.5 gm/dl, accounting for 66.2% of the patients. Mean Hb between 7-9gm/dl was observed in 28.4%) and >10.5 % in 4.1% patients. Only 1.4% patients had mean Hb<7gm/dl.

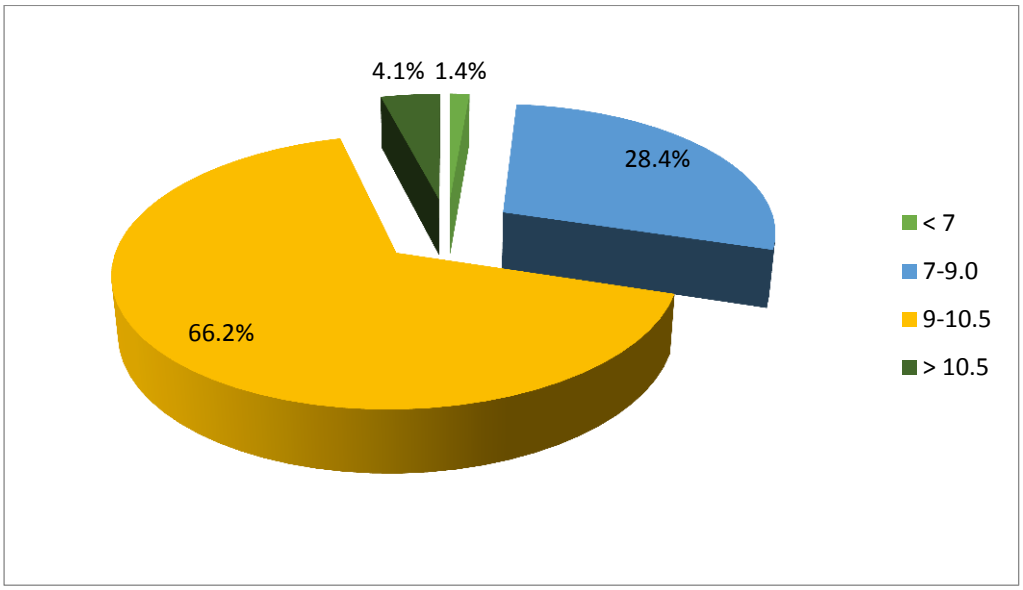

Figure 17: Distribution of average hemoglobin

The average Hb of the study population showed a rising trend from 9.45 ± 0.64 gm/dl during the first year of transfusion to 10.34 ± 0.75 gm/dl over a period of 15 years. There was a fall in mean Hb from the year 2020 - 2022 due to a shortage of leuco-depleted packed cells due to the ongoing COVID pandemic.

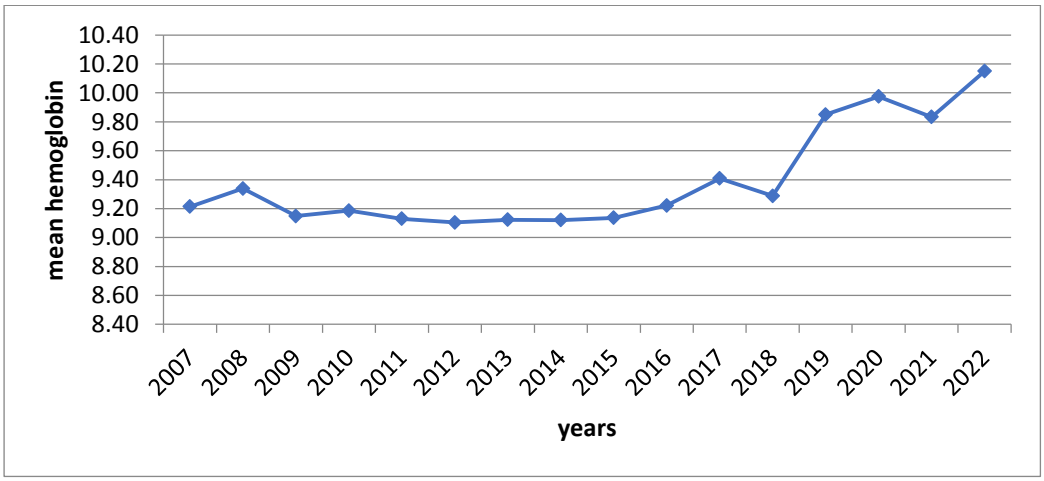

Figure 18: Average haemoglobin trend over the years (2007 - 2022)

All patients were transfused ELISA tested packed red blood cells with or without bedside leucodepletion till 2011, NAT testing was introduced in 2011. Pre-storageleucodepletion for all packed cell units was introduced in 2015 and extended phenotype in 2017.

The average transfusion requirement during the study period was 196 ml/kg/year. The number of patients in different transfusion requirement categories are described as above. Most of the patients (n= 78) had transfusion requirements between 200-250 ml/kg/year. Only one patient had a high transfusion requirement of >300 ml/kg/year attributable to hypersplenism.

Table-9: Transfusion requirement

Transfusion requirement (ml/kg/year)	No. of participants	Percentage (%)
100-200	31	20.9
200-250	78	52.7
250-300	38	25.6
> 300	1	0.8
TOTAL	148	100

The trend in annual transfusion requirement shows a stable trend over the last 15 years. An increase in transfusion requirement was observed in 52 patients (35.13%) with time.

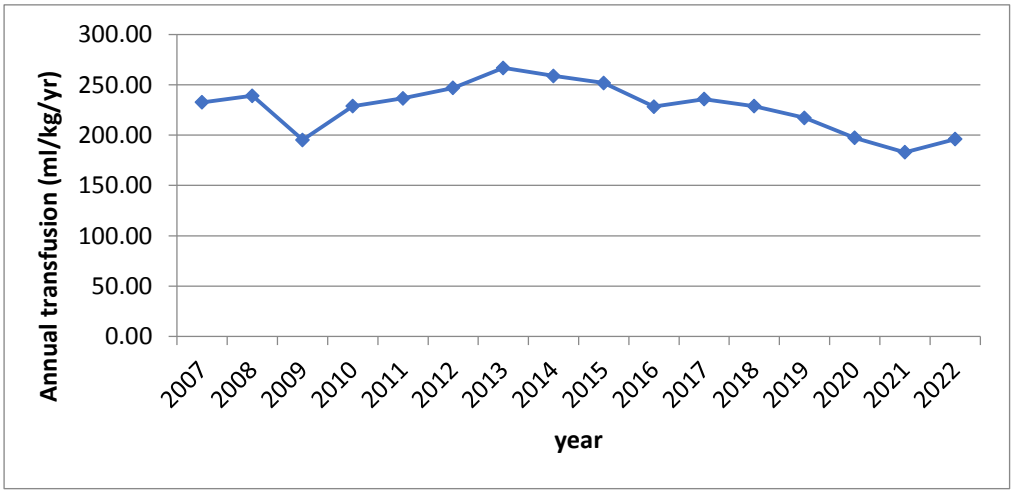

Figure-19: Showing annual transfusion requirement trend

TRANSFUSION TRANSMITTED INFECTIONS:

Annual screening for transfusion-transmitted infections is done as per unit protocol. None of the study participants tested positive for Hepatitis B Antigen. All patients were immunised against hepatitis B virus and had positive Anti Hbs Ag TITRE > 10 IU/ML.

Anti-HCV positivity was found in 6.8% (n=11) patients. All patients with positive Anti -HCV antibodies underwent HCV RNA assessment, which was found to be positive in 4 patients.

The mean viral load was 14,50,000. All these patients were treated with newer antivirals (Sofosbuvir and Daclatasvir) for 12 weeks and only one of the patient achieved a sustained viral response. In the other three patients, viral load is yet to be repeated. Three patients (2%) were found to be positive for anti-HIV and are on antiretroviral therapy.

None of the patients had more than one viral transfusion-transmitted infection.

Two patients (1.4%) had undergone splenectomy at the age of 14 and 16 years due to hypersplenism. Pneumococcal and meningococcal vaccines were administered to both patients before splenectomy as per the unit protocol.

EFFICACY:

IRON OVERLOAD

The iron overloading rate was calculated as per below formula:

[Annual transfusion requirement X 0.6 X 1.08] mg/kg/day 365

Patients were classified based of iron loading rate as low, intermediate, and high. Nearly 90% patients (n=126) had intermediate iron loading rate. Low iron overloading rate was seen in 10 patients and twelve patients had an iron overloading rate of >0.5 mg/kg/day.

Table 10: Distribution of iron overloading rate with age.

		Age group						Total	Chi-square value	p-value
		< 5		5-10.0		> 10				
Iron overload-ing rate	< 0.3	2	5.9%	3	6.5%	5	7.4%	10	8.062	0.089
	0.3-0.5	30	88.2%	35	76.1%	61	89.7%	126		
	> 0.5	2	5.9%	8	17.4%	2	2.9%	12		
Total		34	100%	46	100%	68	100%	148		

Maximum patients had iron overloading rate between 0.3-0.5 despite any iron chelation. Higher mean doses of all three iron chelators was noticed in patients with iron overloading rate <0.3.

Table-11: Showing correlation between iron overload rate and mean dose of different iron chelators

Drugs	Iron overloading rate	N	Mean + Std. deviation
Deferasirox mean dose (mg/kg)	< 0.3	10	33.70 + 6.25
	0.3-0.5	126	31.71 + 6.18
	> 0.5	12	33.92 + 5.98
	Total	148	32.02 + 6.18
Deferoxamine mean dose (mg/kg)	< 0.3	1	70.00 + 9.54
	0.3-0.5	9	34.22 + 23.7
	> 0.5	2	17.50 + 4.95
	Total	12	34.42 + 24.05
Deferiprone mean dose (mg/kg)	< 0.3	3	86.67 + 5.03
	0.3-0.5	28	74.61 + 19.42
	> 0.5	6	77.17 + 14.82
	Total	37	76.00 + 18.06

Maximum patients were having iron overloading rate between 0.3-0.5 and that too maximum had serum ferritin <2500ng/ml n = 90. Out of these 90 patients 9 patients ahd iron overloading rate <0.3 mg/kg/day. Seventy three patients had iron overloading rate between 0.3-0.5 mg/kg/day and 8 patients ahd iron overloading rate >0.5 mg/kg/day. Similarly 50 patients had serum ferritin between 2500-5000 ng/ml ,majority of which (n=43) had iron overloading rate between 0.3-0.5 mg/kg/day. Only 8 patients in baseline had serum ferritin >5000ng/ml.out of which maximum had intermediate iron overload.

Table 12: correlation between iron overloading rate and baseline serum ferritin levels.

		Baseline Serum Ferritin levels groups						Total	Chi-square value	p-value
		< 2500		2500-5000		> 5000				
IRON LOAD	< 0.3	9	10.0%	0	0.0%	1	12.5%	10	**6.431**	0.169
	0.3-0.5	73	81.1%	47	94.0%	6	75.0%	126		
	> 0.5	8	8.9%	3	6.0%	1	12.5%	12		
Total		90	100.0%	50	100.0%	8	100.0%	148		

It was observed that maximum patients were having iron overloading rate between 0.3-0.5 (intermediate range). Majority patients (116) had serum ferritin value <2500 ng/mland 9 patients iron overloading rate <0.3 mg/kg/day. Ninety eight patients had iron overloading rate between 0.3-0.5 mg/kg/day and 9 patients had iron overloading rate >0.5 mg/kg/day.

Twenty eight patients had serum ferritin between 2500-5000 ng/ml, majority of which (n=25) had iron overloading rate between 0.3-0.5 mg/kg/day. Only 4 patients in baseline had serum ferritin >5000ng/ml. Out of which maximum had intermediate iron overload. Overall the baseline and last serum ferritin values remained between 2500-5000 ng/ml and iron overloading rate remained between 0.3-0.5 mg/kg/day.

Table 13: last ferritin and iron overloading rate

		Serum Ferritin levels LAST group						Total	Chi-square value	p-value
		< 2500		**2500-5000**		**> 5000**				
IRON LOADING RATE	< 0.3	9	7.8%	1	3.6%	0	0.0%	10	**2.431**	0.657
	0.3-0.5	98	84.5%	25	89.3%	3	75.0%	126		
	> 0.5	9	7.8%	2	7.1%	1	25.0%	12		
Total		116	100.0%	28	100.0%	4	100.0%	148		

Maximum patients(n= 125) had iron loading rate between 0.3-0.5 and out of them maximum were on deferasirox (n=90) , followed by 27 patients on combination of deferasirox and deferiprone and 8 patients on deferasirox and deferoxamine.

Table 14: Correlation between iron overloading rate and different chelators.

		DEFERASIROX		DEFERASIROX + DEFERIPRONE		DEFERASIROX+ DEFEROXAMINE		Total	Chi-square value	p-value
		No .of cases	Percentage	No .of cases	Percentage	No. of cases	Percentage			
IRON LOADing	< 0.3	7	6.9%	2	5.7%	1	10.0%	10	3.986	0.408
	0.3-0.5	90	89.1%	27	77.1%	8	80.0%	125		
	> 0.5	5	5.0%	5	14.3%	1	10.0%	11		
Total		101	100.0%	35	100.0%	10	100.0%	146		

SERUM FERRITIN:

Over the last 15 years, the average mean ferritin of the study population has decreased from 2566.88 ± 1480 ng/ml at the time of initiation of iron chelation at our unit to 2095.62 ± 1151.98ng/ml at the time of the last assessment

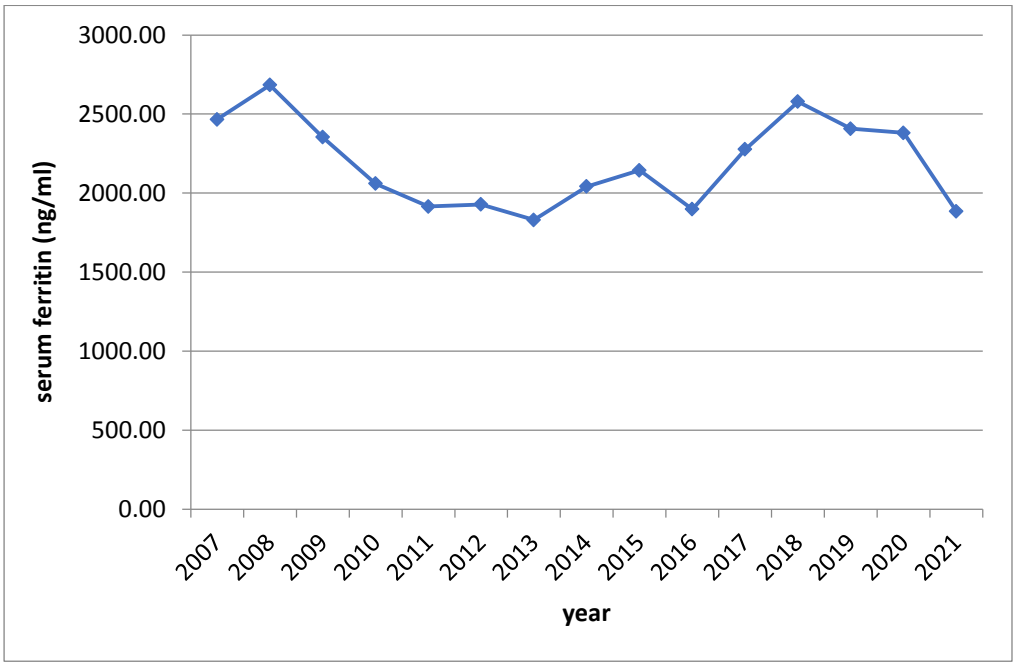

Figure 20: Serum ferritin trend over 15 years

There has been an increase in percentage of patients with serum ferritin below 2500 ng/ml from 60.8% to 78.4% with a corresponding decrease in percentage of patients with serum ferritin between 2500-5000 ng/ml and > 5000 ng/ml.

Table 15: Shows the percentage of patients with serum ferritin in different category.

	Baseline		Last folLow up	
Serum Ferritin levels	No.of cases	Percentage	No.of cases	Percentage
< 2500	90	60.8%	116	78.4%
2500-5000	50	33.8%	28	18.9%
> 5000	8	5.4%	4	2.7%
Total	148	100.0%	148	100.0%

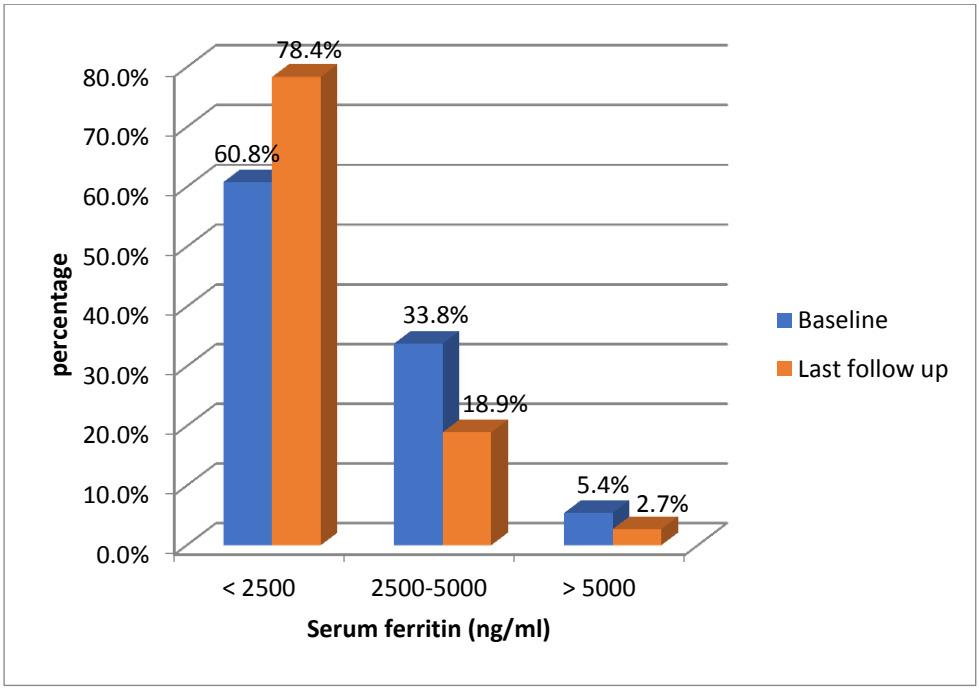

Figure 21: Shows serum ferritin categories (baseline and last follow-up)

The number of patients having baseline serum ferritin value (<2500ng/ml) in <5 years are 23.Thirty patients were in age group 5-10 years and 37 patients were >10 years of age.

In category of 2500-5000 ng/ml, 11 patients are less than <5 years. 13 patients were between 5-10 years and 26 patients were >10 years. There was no patient aged <5 years having serum ferritin >5000ng/ml.

Three patients were between age group 5-10 years and 5 patients were aged >10 years.

Out of total 148 patients, <2500 ng/ml serum ferritin, 35 were female and 55 were male. 14 female and 36 male had serum ferritin between 2500-5000ng/ml.
Three females and 5 males had serum ferritin >5000ng/ml.

Table 16: correlation between serum ferritin (baseline) with age and gender

		Baseline Serum Ferritin levels gp.						Total	Chi-square value	p-value
		< 2500		2500-5000		> 5000				
Age group	**< 5**	23	25.6%	11	22.0%	0	0.0%	34	**4.122**	0.39
	5-10.0	30	33.3%	13	26.0%	3	37.5%	46		
	> 10	37	41.1%	26	52.0%	5	62.5%	68		
Total		90	100.0%	50	100.0%	8	100.0%	148		

		Baseline Serum Ferritin levels gp.						Total	Chi-square value	p-value
		< 2500		2500-5000		> 5000				
Sex	**F**	35	38.9%	14	28.0%	3	37.5%	52	**1.693**	0.429
	M	55	61.1%	36	72.0%	5	62.5%	96		
Total		90	100.0%	50	100.0%	8	100.0%	148		

Table 17: correlation between serum ferritin (final) with age and gender

		LAST Serum ferritin gp (ng/ml)			Total	Chi-square value	p-value
		< 2500	2500-5000	> 5000			
Age group	< 5	28	6	0	34	5.662	0.266
	5-10.0	40	5	1	46		
	> 10	48	17	3	68		
Total		116	28	4	148		
Sex	F	44	8	0	52	3.094	0.213
	M	72	20	4	96		
Total		116	28	4	148		

The number of patients having final serum ferritin value (<2500ng/ml) in <5 years are 28. Forty patients were in age group 5-10 years and 48 patients were >10 years of age.

In category of 2500-5000 ng/ml, 6 patients are less than <5 years. 5 patients were between 5-10 years and 17 patients were >10 years. There was no patient aged <5 years having serum ferritin >5000ng/ml. One patients were between age group 5-10 years and 3 patients were aged >10 years.

Out of total 148 patients, <2500 ng/ml serum ferritin,44 were female and 72 were male. Eight female and 20 male had serum ferritin between 2500-5000ng/ml.Four males had serum ferritin >5000ng/ml.

Table –18 : correlation between serum ferritin (final) with age at enrolment.

		Serum Ferritin levels group						Total	Chi-square value	p-value
		< 2500		2500-5000		> 5000				
AGE AT ENROLMENT IN YEARS	< 2.0	46	51.1%	22	44.0%	6	75.0%	74	**6.547**	0.365
	2-5.0	21	23.3%	8	16.0%	1	12.5%	30		
	5-10.0	16	17.8%	14	28.0%	0	0.0%	30		
	> 10	7	7.8%	6	12.0%	1	12.5%	14		
Total		90	100.0%	50	100.0%	8	100.0%	148		

The patients were divided on the basis of age of enrolment. Patients who enrolled at <2years, 2-5 years, 5-10 years and >10 years of age. Number of patients in <2500 ng/ml. There were total 90 patients whose Serum ferritin was <2500 ng/ml at the time of enrolment, 46 patients were <2 years , 21 patients were between 2-5 years , 16 patients were of age group 5-10 and only 7 patients were >10 years. Fifty patients had serum ferritin between 2500-5000 ng/ml out of them 22 were <2 years , 8 were in age group 2-5 years , 14 had age between 5-10 years and 6 were >10 years. Only 8 patients were having >5000 ng/ml serum ferritin at enrolment maximum were <2 years , 1 was aged between 2-5 years and 1 was >10 years of age.

Table 19: Shows correlation between baseline serum ferritin levels and different ironchelators

		DEFERASIROX		DEFERASIROX + DEFERIPRONE		DEFERASIROX +DEFEROXAMINE		Total	Chi-square value	p-value
		No. of cases	Percent-age	No. of cases	Percent-age	No. of cases	Percent-age			
Baseline Serum Ferritin levels	**< 2500**	72	71.3%	15	42.9%	3	30.0%	90	**20.137**	0.001
	2500-5000	27	26.7%	15	42.9%	7	70.0%	49		
	> 5000	2	2.0%	5	14.3%	0	0.0%	7		
Total		101	100.0%	35	100.0%	10	100.0%	146		

Serum ferritin levels baseline and last values were correlated with iron chelation therapy.

At the initiation of iron chelation, 90 patients had serum ferritin <2500 ng/ml and maximum were on a single drug deferasirox (71.3%). Followed by 49 patients who had serum ferritin between 2500-5000 ng/ml, 15 patients (42.9%) of which were on a combination deferasirox and deferiprone . 7 patients had serum ferritin >5000ng/ml And 5 were on deferasirox and deferiprone. p value is significant.

Table-20 : Shows correlation between last serum ferritin levels and different iron chelators

		DEFERASIROX		DEFERASIROX + DEFERIPRONE		DEFERASIROX+ DEFEROXAMINE		Total	Chi-square value	p-value
		No. of cases	Percentage	No .of cases	Percentage	No. of cases	Percentage			
LAST Serum Ferritin	**< 2500**	82	81.2%	26	74.3%	7	70.0%	115	**4.525**	0.34
	2500-5000	18	17.8%	7	20.0%	2	20.0%	27		
	> 5000	1	1.0%	2	5.7%	1	10.0%	4		
Total		101	100.0%	35	100.0%	10	100.0%	146		

At the last assessment, it was noticed that the number of patients with serum ferritin <2500 had increased to 115 and 7 patients were on deferasirox and deferoxamine as compared to 3 patients at the beginning of assessment. Also, there was subsequent fall in no of patients with serum ferritin 2500-5000 ng/ml and >5000ng/ml. There was over all fall in serum ferritin levels in patients who were complaint and on different iron chelators.

CARDIAC MRI T2*:

Cardiac MRI T2* was done in 8 patients in 2014 and the mean was 36.35 + 4.31 ms. Over the last 9 years, a higher number of patients under went Cardiac MRI evaluation and mean MRTI T2 * in 2022 was 26.40 + 8.94ms.

Table 21: cardiac MRI T2*

CARDIAC MRI -T2/ MIC	N	Mean	Std.
	Valid		Deviation
2022	59	26.40	8.94
2021	27	24.40	6.57
2020	41	26.56	7.93
2019	14	23.62	7.31
2018	20	24.40	11.16
2017	8	24.78	8.39
2016	11	32.61	13.81
2015	4	26.38	10.58
2014	8	36.35	4.31

A stable trend was seen during these years for the cardiac iron overload.

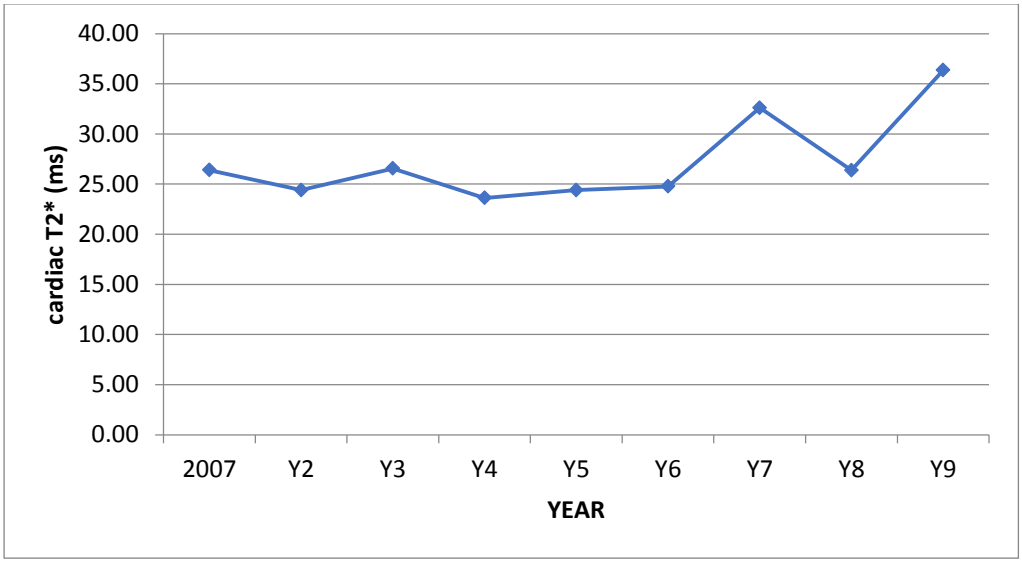

Figure 22: Cardiac MRI T2* trend over nine years.

At baseline (year 2014), there were less number of patients enrolled and the patients >10 years in 2014 had Cardiac MRI T2 value > 20ms. And at the year of last assessment (2022) Total 52 out of 70 patients had MRI T2* value > 20 ms followed by 14 patients having value between 15-20 ms

Table 22: Change in number of patients as per cardiac MRI T2*

	BASELINE		**LAST ASSESSMENT**	
CARDIAC MRI -T2*	**No. of cases**	**Percentage**	**No. of cases**	**Percentage**
< 10	0	0.0%	1	1.4%
10-15.0	0	0.0%	3	4.3%
15-20	0	0.0%	14	20.0%
> 20	8	100.0%	52	74.3%
Total	8	100.0%	70	100.0%

Out of total 70 patients at last year of assessment (2022), The maximum number of patients had MRI T2* value > 20 ms (n= 52). And out of these 52, 26 were <2 years , 9 patients were between 2-5 years, 12 patients were between 5-10 years and 10 patients were >10 years.

Table 23: correlation between age and cardiac MRI T2*

		AGE IN MONTHS gp								Total	Chi-square value	p-value
		< 2		2-5.0		5-10.0		> 10				
CARDIAC MRI -T2*	< 10	0	0.0%	0	0.0%	0	0.0%	1	10.0%	1	10.522	0.31
	10-15.0	2	5.9%	0	0.0%	0	0.0%	1	10.0%	3		
	15-20	6	17.6%	1	10.0%	4	25.0%	3	30.0%	14		
	> 20	26	76.5%	9	90.0%	12	75.0%	5	50.0%	52		
Total		34	100.0%	10	100.0%	16	100.0%	10	100.0%	70		

Maximum patients having MRI T2 * >20 ms were on deferasirox (n= 33), 15 patients were on combination of deferasirox and deferiprone and 4 were on deferasirox and deferoxamine.

Table 24: correlation between Cardiac MRI T2 * and iron chelators.

		DEFERASIROX		DEFERASIROX + DEFERIPRONE		DEFERASIROX +DEFEROXAMINE		Total	Chi-square value	p-value
		No. of cases	%	No. of cases	%	No. of cases	%			
CARDIAC MRI -T2*	< 10	0	0.0%	1	5.3%	0	0.0%	1	9.043	0.171
	10-15.0	0	0.0%	1	5.3%	1	14.3%	2		
	15-20	10	23.3%	2	10.5%	2	28.6%	14		
	> 20	33	76.7%	15	78.9%	4	57.1%	52		
Total		43	100.0%	19	100.0%	7	100.0%	69		

The trend of cardiac iron overload during the years depicts that in 2014 the patients enrolled were all having MRI T2 * value >20 ms, over the years as the no. of patients enrolled increased, there was deterioration of MRI cardiac T2 * value trend . It can be explained by the fact that the patients of different socio-economic status started enrolling and the values started varying during the course of years.

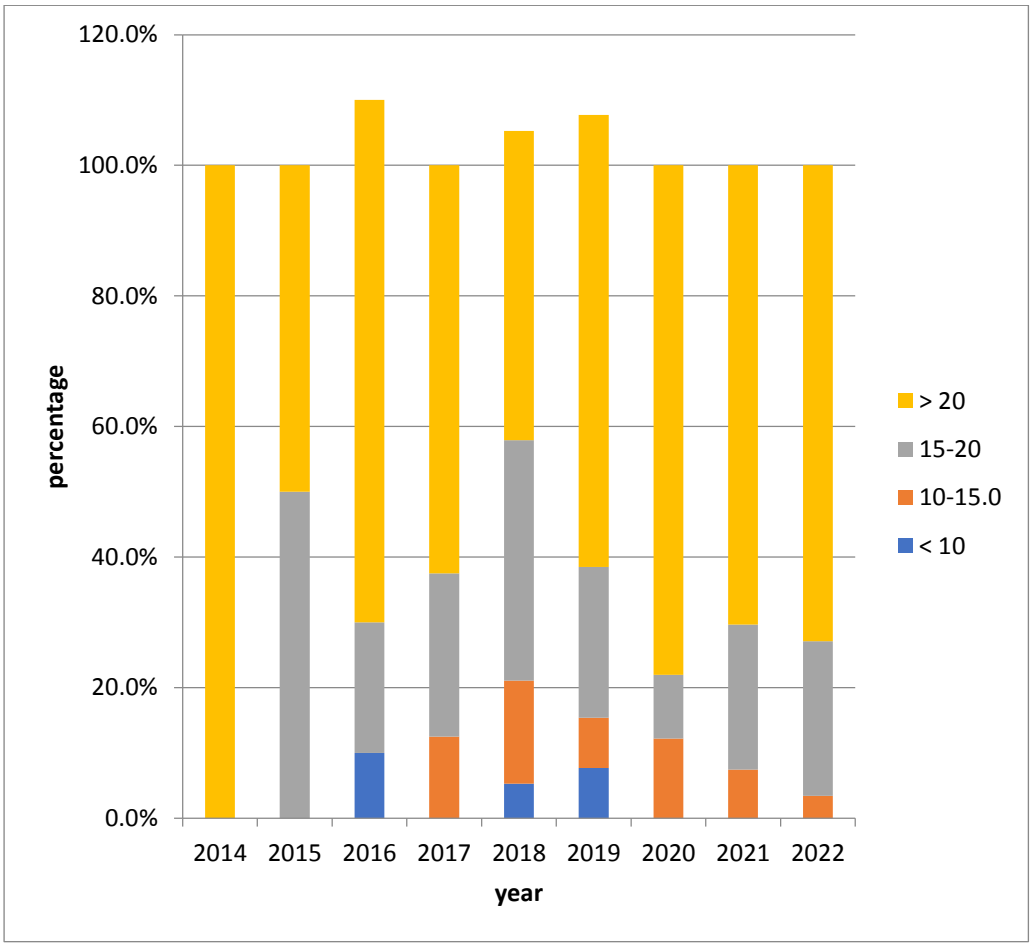

Figure 23: Trend and Distribution of cardiac MRI T2* values over the years.

LIVER IRON CONCENTRATION:

Liver MRI was done in 9 patients in 2014 and the mean LIC was 7.39 + 5.02 mg/g dry weight of liver. Over the last 9 years, a higher number of patients under went Liver MRI evaluation and mean LIC in 2022 was 6.94 + 4.84 mg/g dry weight.

Table 25: Average liver iron concentration trend over years

LIVER MR	LIC	Mean	Std. Deviation
	Valid		
2022	58	6.94	4.84
2021	28	6.02	4.71
2020	40	6.99	4.64
2019	13	6.96	4.32
2018	18	6.88	5.07
2017	10	5.70	3.48
2016	10	8.33	8.10
2015	2	4.00	4.25
2014	9	7.39	5.02

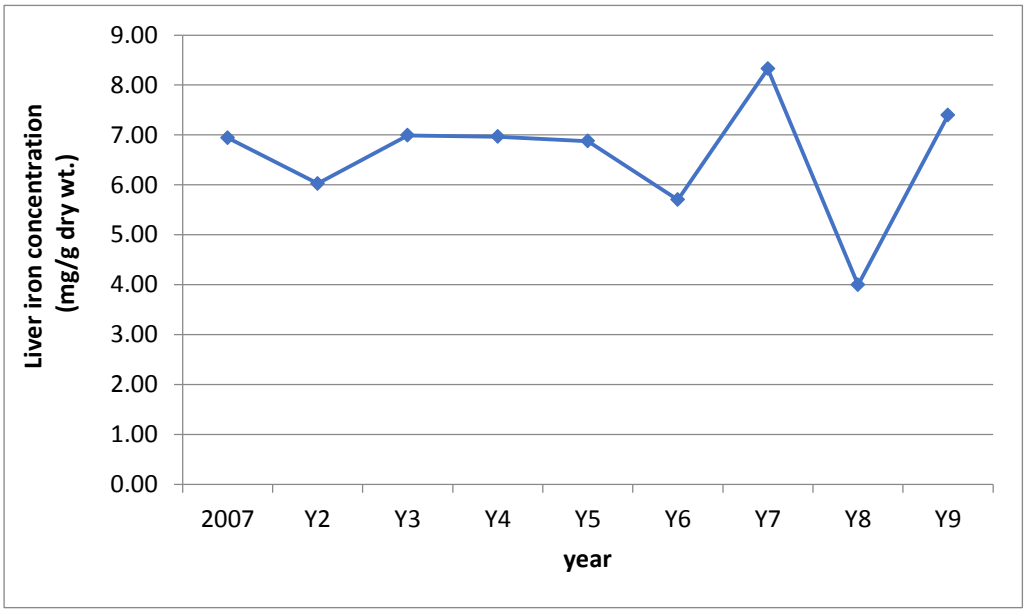

Figure 24: Liver MRI trend over years

At baseline (year 2014), there were less number of patients enrolled and 9 patients >10 years in 2014 had liver MRI evaluation and 4/9 patients had LIC – between 3-7 mg/g dry weight. And at the year of last assessment (2022) Total 23 out of 69 patients had LIC 7-15 mg/g dry weight followed by 22 patients having value between 3-7 mg/g dry weight.

Table 26: Change in number of patients as per liver iron concentration.

	BASELINE		**LAST ASSESSMENT**	
LIVER MRI LIC	**No .of Cases**	**%**	**No. of cases**	**%**
< 3	1	11.1%	19	27.5%
3-7.0	4	44.5%	22	31.9%
7-15.0	3	33.3%	23	33.3%
> 15	1	11.1%	5	7.3%
Total	9	100.0%	69	100.0%

Maximum patients (n=15) were having LIC3-7 mg/g dry weight were on deferasirox,7 patients were on combination of deferasirox and deferiprone having LIC<3 mg/g dry weight and 4 were on deferasirox and deferoxamine and had LIC>7-15 mg/g dry weight .

Table 27: correlation between LIC and iron chelators

		DEFERASIROX		DEFERASIROX + DEFERIPRONE		DEFERASIROX +DEFEROXAMINE		Total	Chi-square value	p-value
		No. of cases	%	No. of cases	%	No. of cases	%			
LIVER MRI LIC	< 3	10	23.8%	7	36.8%	2	28.6%	19	4.119	0.661
	3-7.0	15	35.7%	6	31.6%	1	14.3%	22		
	7-15.0	13	31.0%	5	26.3%	4	57.1%	22		
	> 15	4	9.5%	1	5.3%	0	0.0%	5		
Total		42	100%	19	100%	7	100%	68		

The trend of LIC during the years depicts that in 2014 the maximum patients were having value between 3-7 mg/g dry weight compared to 2022, at the last year of evaluation almost same percentage of patients had LIC between 7-15 and 3-7 mg/g dry weight of liver (n= 22) for each category.

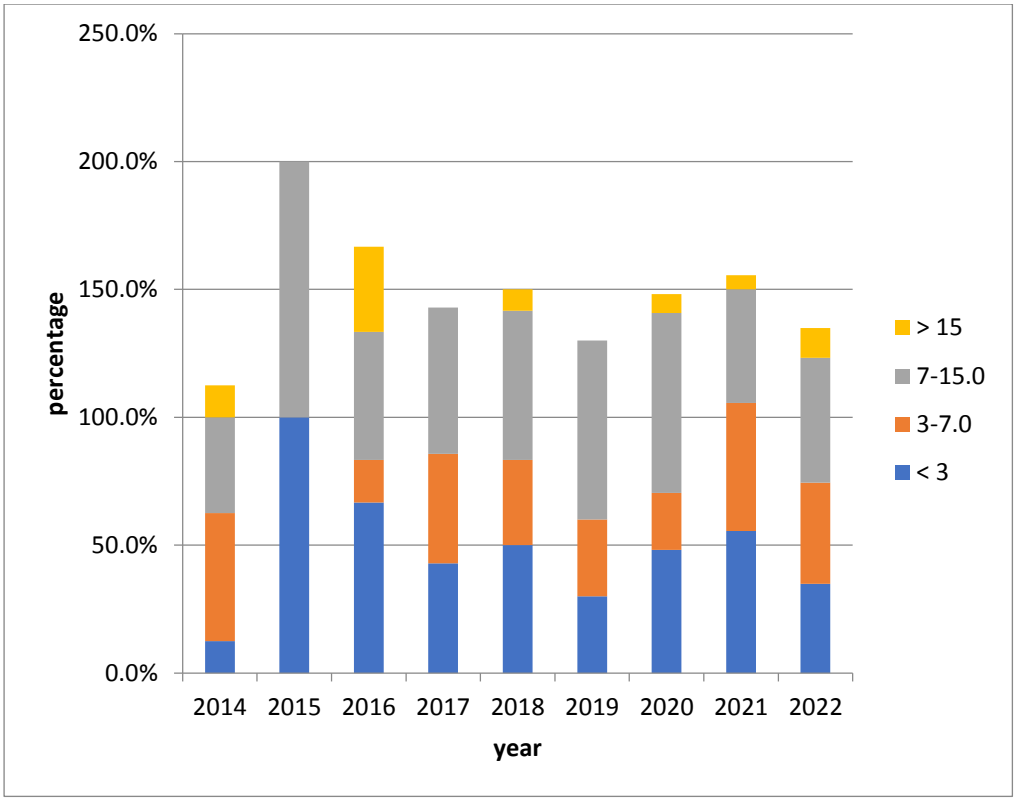

Figure 25: Trend of changing LIC over the years

Iron chelation

C. DOSING AND DURATION:

The study included 148 patients with TDT on iron chelation therapy. At the time of assessment, 101 (68.2%) patients were on chelation with single agent deferasirox and 47(31.8%) patients were on different combinations of ICT.

Table 28: Distribution of drugs

DRUG	No. of cases	Percentage
Deferasirox	101	68.2%
Deferasirox + deferiprone	35	23.6%
Deferasirox + deferiprone + deferoxamine	2	1.4%
Deferasirox +deferoxamine	10	6.8%
Total	148	100.0%

The different combinations of the ICT used were:
combination of deferasirox and deferiprone in 35 patients (23.6%) and deferasirox and deferoxamine in 10 (6.8%) patients. All three iron chelators were being used in 1.4% patients.
The reasons for starting combination therapy in 47 patients were as follows:

- Persistently high serum ferritin in spite of maximum doses of single iron chelator- 26(61.9%).
- Cardiac iron overload leading to the addition of deferiprone or deferoxamine-11(23.4%).
- IncreasingLIC on the maximum dose of DFX -7 (14.8%).
- Inability to administer the desired dose of single chelator due to adverse effects – 3(6.3%).

The mean doses and average duration of exposure of each iron chelator is shown in graph. The mean dose of deferasirox was 32.02

+6.18 mg/kg/day (Range 16-43 months) and mean duration of exposure was 56.39+40.13 months. The mean dose for Deferoxamine was 34.42 +14.05 mg/kg/day (Range 14-96 months) with average duration of exposure of 40.25 months. The mean dose for Deferiprone 76 + 18.06 mg/kg/day (Range 20-96 months) and average duration of exposure of 53.86 +40.58 months.

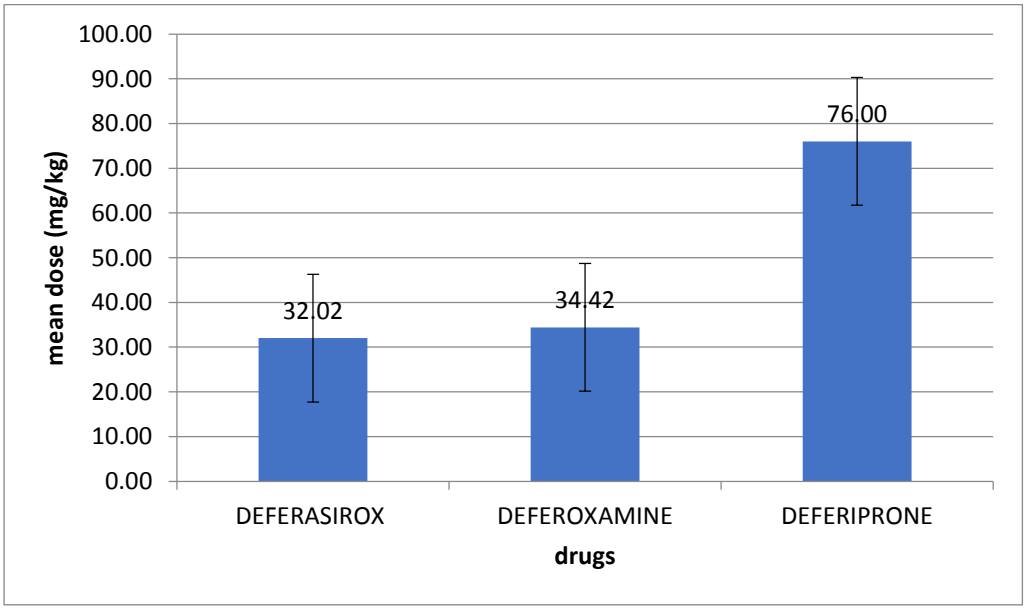

Figure 26: Mean dose of iron chelators

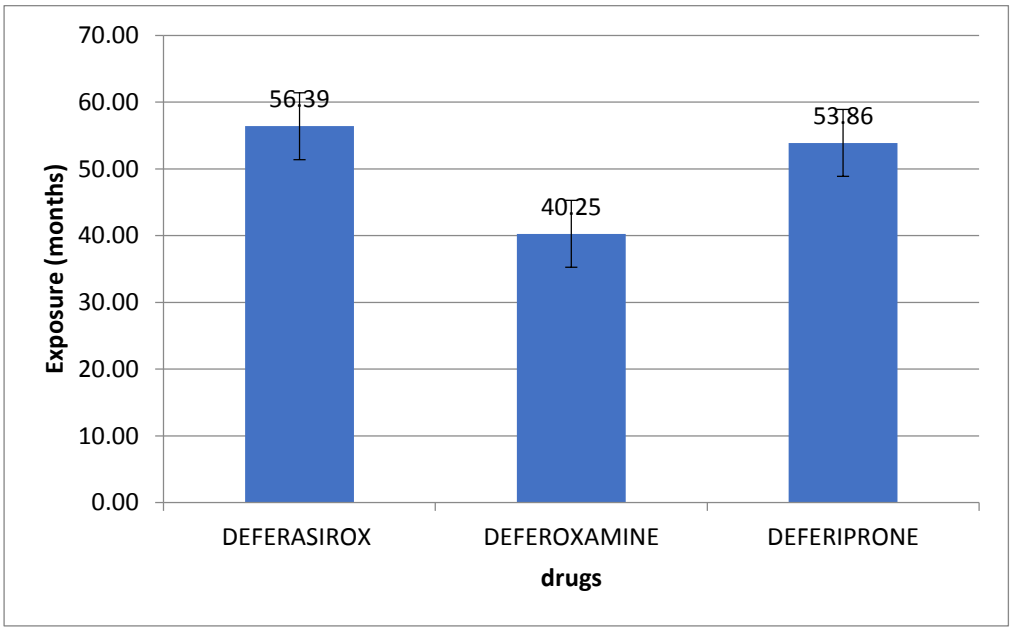

Figure - 27: Months of exposure with standard duration for iron chelators

The mean dose of deferasirox when used as a single agent was higher (39.45 mg/kg/day) as compared to (28.78mg/kg/day) when used in a combination.

Table -29: Showing mean dose of deferasirox as a single and in combination.

DEFERASIROX	Single		Combination		Z	p-value
	Mean	SD	Mean	SD		
MEAN DOSE (mg/kg)	31.44	6.03	33.28	6.37	-1.699	0.091

The mean dose of deferasirox was > 30 mg/kg/d in 68.9% patients, 20-30 mg/kg/d in 27.7% patients and 5 patients (3.4 %) received a mean dose <20 mg/kg.

Table- 30: Mean doses of deferasirox

DEFERASIROX DOSE GROUP	No. of cases	Percentage
< 20	5	3.4%
20-30	41	27.7%
> 30	102	68.9%
Total	148	100.0%

E. SAFETY AND TOLERABILITY:

The bar graph below shows the number of patients who experienced adverse effects with ICT:

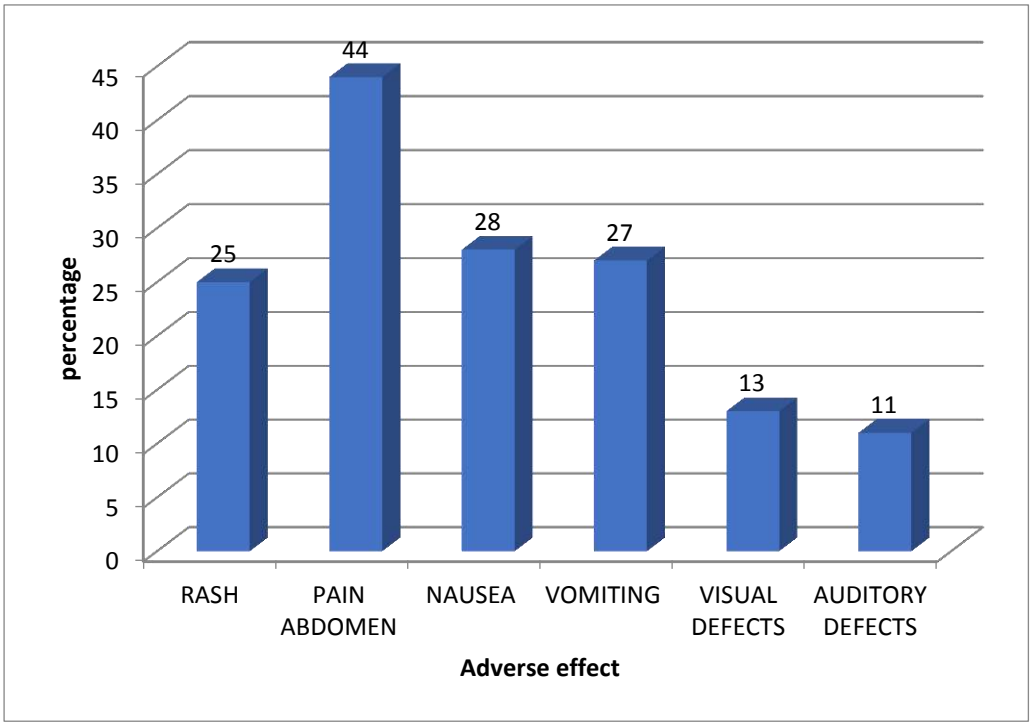

Figure 28: Shows different clinical adverse effects

RASH

Skin rash was observed in n= 25 (16.9%) of participants, which resolved with symptomatic management and did not lead to permanent drug discontinuation in any of the participants. The severity of rash was grade 1 and grade 2 in 3.4 % and 13.5% patients respectively. No grade 3 or grade 4 events were seen.

GI SYMPTOMS - Most common was pain abdomen n= 44 (29.7%) followed by nausea n= 27 (18.9%) and n= 28 vomiting (18.2%).

VISUAL DEFECTS

Only 8.8 % (13 patients) had mild visual defects. 12 patients had myopia and 1 had macularedema (grade 1).No drug was modified due to visual defects.

AUDITORY EFFECTS:

Eleven patients (7.4%) had mild auditory defects. None had sensorineural hearing loss and no drug modification was done.

Haematological abnormalities were seen in 96patients:

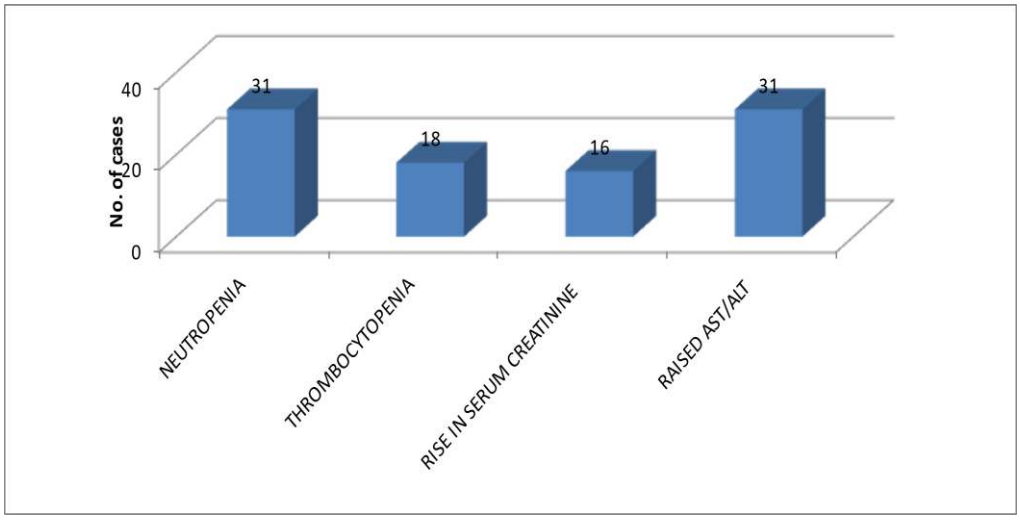

Figure 29: Laboratory parameters of adverse effects

NEUTROPENIA:

Total thirty- one patients had neutropenia in total out of which 18.2% (n=26) had grade 1 neutropenia (ANC LLN-1500 / microliter.) and 2.7% (n= 5) (had grade 2 neutropenia (ANC between 1500- 1000/ microliter. None of the patient's experienced grade 3 or 4 neutropenia.

THROMBOCYTOPENIA:

Out of a total of 148 patients, only 18 patients had thrombocytopenia. 3 patients (2%)- had grade 1 Thrombocytopenia- >75000/microliter and 10.1% (n= 15)had grade Thrombocytopenia - by the way, 50000-75000/microliter.

Raised AST/ALT:

34 patients had developed transaminitisout of which 17 patients (11.5%) - had grade 1 rise with AST/ALT (>1.5-5 ULN), 13 patients (8.8%) had grade 2 rise with AST/ALT >5-10 ULN. Only one patient (0.7%) had grade 3 rise with rise in AST/ALT >10 ULN.

Raised creatinine:

16 patients (10.8%) had raised creatinine. 10 patients had grade 2 rise and 6 patients had grade 1 raised creatinine.

According to the below graph, neutropenia and thrombocytopenia are caused maximum by a combination of deferasirox and deferiprone.

Rise in creatinine and transaminases are caused maximum in patients on deferasirox and deferoxamine

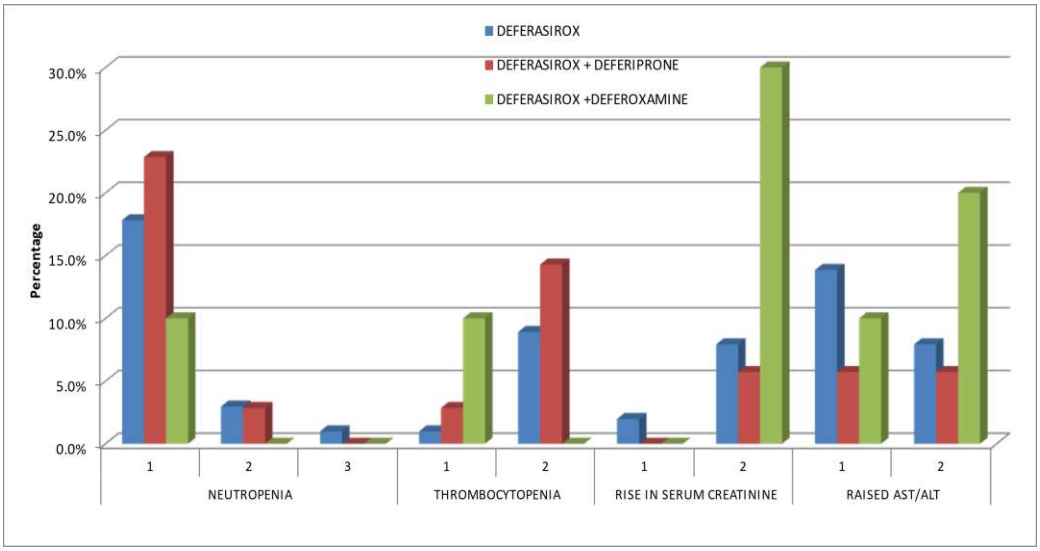

Figure 30: Shows different drugs causing different adverse effects.

Amongst the entire cohort of 146 patients on, 58 patients tolerated the iron chelation therapy well and dose reduction was not required where as in 88 patients, there was need for dose reductions due to various reasons. Out of 88 patients, there were 49 patients in whom dose of Deferasirox was reduced as their serum ferritin reduced,13 had proteinuria ,10 had raised creatinine and 16 had raised liver enzymes hence dose was reduced. Permanent with-drawl of drug was required in only 4 patients but remaining 84 patients continued with the iron chelation.

Figure 30: Shows dose reduction of the drugs

COMPLIANCE:

Poor compliance to ICT was documented in medical records of only 12.2 % patients (n=18).

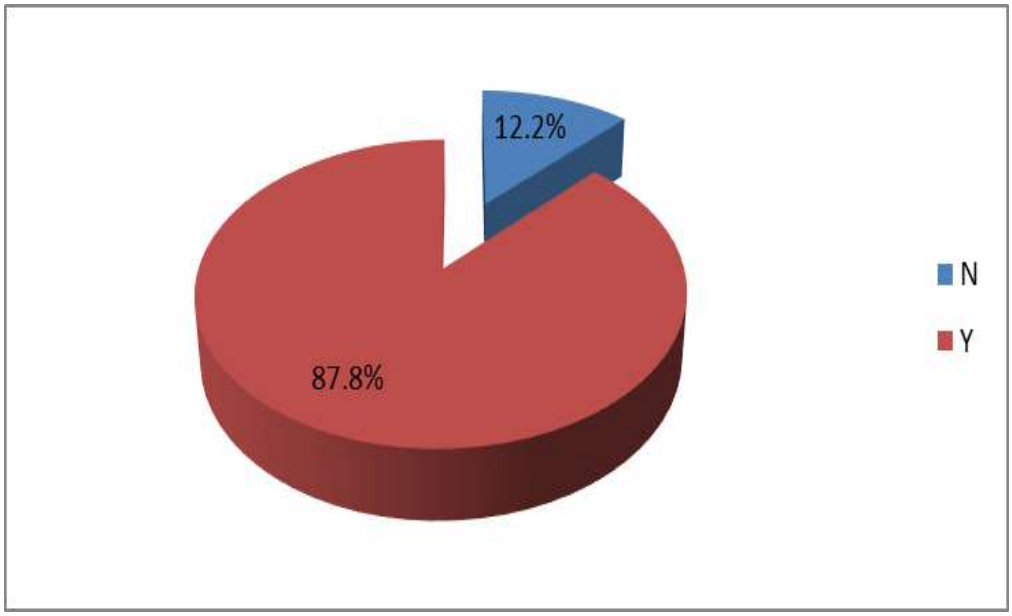

Figure 31: COMPLIANCE

Two patients were excluded (who were on all three iron chelatorcombinations.

Out of 101 patients who were on the single drug (deferasirox), 89 patients complaint of deferasirox accounting for 88.1%, and 12 were non-compliant (11.9%).There were 35 patients receiving a combination of both deferasirox and deferiprone. only 5 patients were non-compliant, majority were compliant (n= 30) accounting for 85.7% of patients. Only 10 patients were receiving deferasirox and deferoxamine and 100 % compliance was seen.

Table 31: Shows the correlation between compliance and different iron chelators for 146 patients.

		DEFERASIROX		DEFERASIROX + DEFERIPRONE		DEFERASIROX+ DEFEROXAMINE		Total	Chi-square value	p-value
		No. of cases	%	No. of cases	%	No. of cases	%			
COMPLIANCE	N	12	11.9%	5	14.3%	0	0.0%	17		
	Y	89	88.1%	30	85.7%	10	100.0%	129	**1.561**	0.458
Total		101	100%	35	100%	10	100%	146		

DISCUSSION

The transfusion of packed red blood cells is the cornerstone in the treatment of TDT. Patients with TDT after regular transfusions develop tissue iron overload which results in significant mortality and morbidity.[39] To this iron overload or hemosiderosis, iron chelation therapy is the answer. Iron chelation therapy as a single oral agent or in various combinations reduces the overall iron burden and improves the quality of life in thalassemia patients. [40] The burden of excessive transfusions is directly proportional to the frequency, volume, and duration of blood transfusions. Iron excess if remains untreated can cause several side effects, including hepatic and cardiac dysfunction and failure.[41]

This is an observational study conducted during the study period (from 1st July 2021 to 31st December 2022), and 148 patients were evaluated over these 15 months. All the patients received iron chelation therapy. Their respective records were studied and different laboratory and clinical parameters like serum ferritin, liver enzymes, serum creatinine, growth, iron overload, transfusion requirements, average Hb, and chelation-related adverse effects etc were compared for their safety and efficacy.

BASIC DEMOGRAPHIC DETAILS:

AGE: In our study, the mean age plus standard deviation for all patients was determined to be 9 years 3 months with a range of 6 months to 17.5 years. Similar studies with comparable results like The Escalator experiment by TaherA. et al [42] included 237 patients, with a mean age of 13.2 years and a range of 2-42 years. Out of them, 162 were pediatric patients with an average age of 9.5 years, ranging from age of 2 to 16 years. Another phase III study of deferasirox was conducted by Cappellini MD et al [27] 51%of patients were <16 years old, and the majority of them received one year of medication. In a parallel study by Gomber S et al, 49 children were evaluatedand the

meanage of patients was 11.6 (6.21) years.[44] In another research by Merchant R et al, 30 patients were evaluated and the patients had a mean age of 7 years (range 6.5 to 29 years).

GENDER

Our study included 96 (64.8%) males and 52 (35.1%) females. A study by Gomber S et al included 49 patients, and out of a total 30 (61.22%) were men and 19 (38.78%) were women.[43] There were 27 (40.3%) male and 40 (59.7%) female patients in the Cassinerio E et al. study.[44] In the phase III research by Cappellini MD et al,[45] 51.9% of the patients were female.

SERUM FERRITIN:

Serum ferritin broadly correlates with body iron stores and can be easily measured**.** Iron burden should be assessed by monthly measurement of serum ferritin levels, and the dose of ICT , The need to switch or escalate or rather reduce the dose depends upon the serum ferritin value. During our study, the serum ferritin was repeated three months and dose if need be adjusted. The mean value of serum ferritin in patients evaluated our unit decreased from 2566.88 ± 1480 ng/ml at the time of initiation (2007) of iron chelation at our unitto 2095.62 ± 1151.98 at the time of last assessment (2022). In this investigation, the baseline serum ferritin levels in the groups of the current study were comparable. The values of mean last values (+standard deviation) were 1863.53 + 854.91 ng/ml in the Deferasiroxgroup, 2170.46 +1568.7ng/mL in the Deferasirox and deferiprone group, and 2678.9 +1433.93ng/mL in the Deferasirox plus deferoxamine group. It suggests that deferasiroxtreatment is similarly effective on the SF level as combination therapy (deferiprone + deferoxamine and deferasirox and deferoxamine. In a study by MouradFH et al,[29] serum ferritin levels were evaluated in 14 patients receiving deferasirox, a falling trend of serum ferritin was seen from 5506 + 635 ng/ml to 4856 + 699 Ng/l at 6 months (P 0.001) and to 3998 + 604 ng/l at 12 months (P 0.001). Other studies that produced

various findings as follows : The meta-analysis by Xia S et al.[46] showed that in eleven patients receiving daily deferiprone and DFX, serum ferritin levels dropped from 4153 + 517 ng/l to 3005 + 393 ng/l at 6 months (P 0.001) and to 2805 + 327 ng/l at 12 months (P 0.01). In the study by Lal A et al,[47] patients were divided into two groups A and B, Group A which had moderate iron overload (N=18) had median blood ferritin values of 1,510 ng/mL as compared to group B (4,750 ng/mL) having severe iron overload (p=0.002). A drop in median serum ferritin was observed to be 24%. Also, a relationship was found between serum ferritin and liver iron concentration i.e. as the serum ferritin increased, the liver iron concentration also increased. A study by Farmaki K et al.[48] which was conducted among 16 patients over two years. The study showed that the serum ferritin estimated the total iron burden and ferritin decreased along with LIC and MRI T2*. In another study by Gomber S et al,[43] the mean serum ferritin values were analysed, at 6 months, and 12 months. The blood ferritin levels were comparable at baseline and there was a fall in serum ferritin levels in all three groups after chelation therapy for 6 and 12 months. Serum ferritin fell more quickly in the combination (deferiprone and deferasirox) group than in groups 1 and 2 (P=0.035 and P=0.04, respectively). In the study by Chang HH et al [49] conducted for 7 years on patients who were on deferasirox, the patients' mean serum ferritin levels dropped significantly from 4279 ng/mL at the start of deferasirox treatment to 1713 ng/mL at the end of treatment.

MRI T2* and LIC

MRI T2*Heart and Liver MRI LIC have now emerged as a prominent marker for assessing cardiac iron overload and liver iron concentration. These tests are more feasible due to their non-invasive nature when compared to biopsy and hence have better compliance among the patients. In our study, MRI T2* and LIC were repeated annually in patients >10 years. Cardiac MRI T2* was done in 8 patients in 2014 and the mean was 36.35 + 4.31 ms. Over the last 9 years, a higher

number of patients under went Cardiac MRI evaluation and the mean MRTI T2 * in 2022 was 26.40 + 8.94ms.

It can be explained by the fact that patients of different socio-economic statuses started enrolling and the values started varying over years. Maximum patients having MRI T2 * >20 ms were on deferasirox (n= 33), 15 patients were on a combination of deferasirox and deferiprone and 4 were on deferasirox and deferoxamine.Liver MRI was done on 9 patients in 2014 and the mean LIC was 7.39 + 5.02 mg/g dry weight of the liver. Over the last 9 years, a higher number of patients underwent Liver MRI evaluation and the mean LIC in 2022 was 6.94 + 4.84 mg/g dry weight.

The levels were higher in all three groups of chelators in the follow-up MRI performed after 15 months of ICT, which was suggestive of a decreased iron load on the liver. Despite the reduced iron burden, the findings were still regarded as mild hepatic iron overload. The results of our current study showed parallelism with those of other studies: In the meta-analysis by Xia S et al,[46] conducted randomized controlled trials for studying the effect of LVEF and MRI T2* and it was found that deferiprone mono- and combination therapy to be more superior in improving cardiac function than deferoxamine therapy. Deferoxamine alone was shown to be less effective. In the study by Cassinerio E et al,[44] 67 patients were evaluated who were on various chelation regimens. These patients underwent T2* cardiovascular magnetic resonance at baseline , after 6–14 months , and after 32 months (t2). The chelation therapy was divided amongst the patients into four groups: group A received deferasirox, group B - deferoxamine, group C - combination therapy, deferoxamine + deferiprone, and group D - deferiprone (deferiprone alone). Myocardial T2* at the beginning varied between 10 and 20 ms in 22 individuals and between 20 -30 ms in 37 patients, with an average of 10 ms occurring in 8 cases. Alterations were observed in T2*between 6-14 months and after 32 months of interval study. Three patients from group B, ten from group A, and three from group C showed normalizing pattern of cardiac iron overload.

Similarly in another study by Gomber S et al, [43] patients showed baseline liver MRI T2* values suggesting moderate hepatic iron overload. The follow-up MRI indicated minor hepatic iron excess after six months of treatment. At baseline and follow-up, heart MRI T2* individual and mean values were almost the same.

MEAN DOSES:

In our current study cohort, the patients were on different iron chelators. All the patients had received at least one dose of deferasirox. No patient was solely on deferiprone. DFX+ DFP was started in 35 patients and DFX N DFO in 10 patients. All three chelators were used in 2 patients only. And 101 patients were on deferasirox. The mean doses and average duration of exposure of each iron chelator. The mean dose of deferasirox was 32.02 +6.18 mg/kg/day (Range 16-43 months) and the mean duration of exposure was 56.39+40.13 months. The mean dose for Deferoxamine was 34.42 +14.05 mg/kg/day (Range 14-96 months) with an average duration of exposure of 40.25 months. The mean dose for Deferipronewas 76 + 18.06 mg/kg/day (Range 20-96 months) and the average duration of exposure of 53.86 +40.58 months.

In the experiment by Tanner MA et al,[50] deferoxamine and deferiprone were given a mean dose of 38 + 10.2 mg/kg for 5.3 days per week and 73.9 + 4.0 mg/kg per day, respectively. Other studies with comparable findings are- deferasirox (30 mg/kg) and deferoxamine (average daily dose 51 mg/kg) both decreased liver iron concentration by 8.9 mg/g/dry weight and 6.4 mg/g/dry weight, respectively. In a study by Karami H et al,[51] deferiprone and deferasiroxat doses of 53.922.2 and 29.36.8 mg/kg/day, respectively. In combination therapy, various doses of deferiprone and deferasirox Were given based on the patient's clinical state and laboratory findings. In the study by Totadri S et al,[52] the mean doses of deferiprone and deferasirox were 84.45.2 (range 61-100 mg/kg/day) and 33.45.2 (range 20-40 mg/kg/day), respectively.

ADVERSE EFFECTS:

Various adverse effects were seen after starting treatment with different iron chelators as monotherapy or in combination. In our study the adverse effects were divided into clinical and laboratory parameters. Adverse effects were graded as per CTCAE version 5. Most common was pain abdomen n= 44 (29.7%) followed by nausea n= 27 (18.9%) and n= 28 vomiting (18.2%) and pain abdomen (29.7%). Rash was seen in 16.9% patients, nausea in 18.9% and vomiting in 18.2%. Only 8.8 % (13 patients) had mild visual defects. 7.4 % patients had mild auditory defects. Thirty-one patients had neutropenia and 18 patients had thrombocytopenia. Thirty four patients had de-arranged LFT's and 16 patients (10.8%) had raised serum creatinine levels. Rise in creatinine and transaminases were found to be caused maximum in patients who were on deferasirox and deferoxamine. There were no deaths amongst our patients during this study period. Permanent with-drawl of drug was required in only 4 patients but remaining 84 patients continued with the iron chelation.

Our study confirmed other studies that show excellent responses in reducing organ specific iron load and improving quality of life with the use of the combination of DFO and DFP and that similar results are possible with the combination of DFP and DFX. Also, it strongly suggested, that because of better compliance with the two oral chelators, the efficacy in reducing iron load is superior to that of one oral and one parenteral. MuzamilShabanaEjaz, et al [53] conducted a study on pediatric patients for the comparison of adverse effects with duration of ICT . It was observed that below 36 months of optimal chelation abdominal pain was 35%, nausea 21%, vomiting 7%, jaundice, 8% anemia was present in 47% patients whereas above 60 months, abdominal pain was 3%, nausea 5% vomiting 3%. Jaundice 2% and anemia, 5% showing that as the duration of chelation increases the severity of adverse effects decreases.

Nuzi et al [54] conducted a study on relation of ICT with ocularfunction inpatients and it was observed that there was no relation between ICT and visual conditions like lens opacities, retinal diseases, optical neuropathies, astigmatism, visu al field and RNFL thickness defects.

H. Sarbay, et al [55] conducted a case study for adverse effects related to deferasirox, nephrotoxicity is one of the common side effects in the form of nephritis and tubulopathy. In a complete urine analysis, proteinuria 3+ was detected and spot urine/creatinine ratio came out to be 2.5.

M. Domenica Cappellini, et al [45] conducted a study for 5 years. It was concluded that the most common drug-induced events were increased serum creatinine in 11.2%, abdominal pain in 9.0%, and nausea in 7.4%. These adverse effects were mild to moderate and transient. No adverse effect was observed on pediatric growth or adolescent sexual development.

Wan Jin Lee, Nurul Ain,MohdTahir et al [56] conducted a study which drew a relationship between compliance and prevalence of adverse effects like auditory , visual impairment, bony abnormalities, growth retardation, skin allergies are recognized as the side effects related to DFO. Furthermore, at higher doses, neurological, and pulmonary issue have been observed in some patients. Agranulocytosis, and gastrointestinal issues were seen more in patients on DFP. Meanwhile, patents prescribed with DFXhad most commonly experienced gastrointestinal effects, a rise in serum creatinine, and skin rashes.

COMPLIANCE

During the study in our cohort, compliance was checked by verbally asking either the patients or their parents (in children <12 years).Poor compliance to ICT was documented in medical records of only 12.2 % patients (n=18).

Our study concluded that clinically, good compliance to ICT has a good impact on disease control and the quality of life in thalassemia patients. A high level of compliance is associated with significantly lower serum ferritin levels which lowered the risk of iron overload-related complications, as well as a better quality of life. Mokhtar et al. (2013) [57] conducted a study concluded that significantly high incidence was seen of impaired left ventricular contractility in the non-compliant group (p=0.021). The MRI finding reported in the study by Sukhmani et al. (2020) [58] revealed that non-compliant patients tend to have cardiac and severe hepatic overload also, compliance significantly reduces cardiac iron overload and cardiac complications.

SUMMARY AND CONCLUSION

During the study period of 15 months, a total of 148 patients were studied who came for regular transfusions in the Thalassemia ward of the hospital. All patients were on single or more iron chelation therapy. Their records were evaluated for efficacy and safety measures.

DEMOGRAPHICS:

- The mean age was 9.3 years with a range of 6 months to 17.5 years.
- Nearly half (45.9%) of patients were > 10 years of age. Patients between 5-10 and < 5 years constituted 31.1% and 23% of the study population respectively.
- The male-to-female ratio was 1.84:1.
- Underweight patients and patients who were obese
- The mean age at diagnosis of TDT was 8.19 ± 3.8 months
- The mean age of enrolment at TDCC was 41.9 ± 42.8 months (Range – 3mon – 17 years).
- The average age at starting iron chelation was 58.06 ± 40.23 months(Range – 10 - 204 months).
- 109 (73.6%) study participants resided in an urban area whereas 26.4% (n=39 patients) were rural dwellers.
- Most patients (35.8%) belong to the lower middle class followed by the upper middle-class accounting for 33.1%.
- B positive was the commonest blood group (35.1%) and A- and AB- were the least common blood groups (0.7% in each group).
- Maximum proportion of patients 66.2%, had Hb between 9-10. 5 gm %.
- 33.1 % of the patients were undernourished (<3rd centile), and 55.4 % were between the 3rd -and 97th centile.
- Weight was > 97th centile in 11.5% of the study participants.
- Short stature was present in 27 % of participants.

- The maximum percentage of patents (47.8%) fell in the category of 50-97th centile and belonged to the age group between 5-10 years

Normal onset and progression (grade-1) was seen in a maximum percentage of (55.9%) patients (n= 38). Delayed puberty was seen in 9 patients (13.2%). The pubertal arrest was seen in 13 patients (19.1%). Pubertal failure was seen in 8 patients (11.8%)

INVESTIGATIONS:

- The average Hb was maintained between 9-10.5 and accounted for 66.2% of the patients.
- Only 1.4% of patients had mean Hb<7.
- Most of the patients (n= 78) had transfusion requirements between 200-250 ml/kg/year.
- Maximum patients (n= 126) had an iron overloading rate between 0.3-0.5 ml/kg/year in all age categories.
- All patients were immunized against the hepatitis B virus and had positive Anti Hbs antigen titer> 10 IU/ML.
- HCV-RNA assessment, which was found to be positive in 4 patients.
- The average mean ferritin of the study population has decreased from 2566.88 ± 1480 ng/ml at the time of initiation of iron chelation at our unit to 2095.62 ± 1151.98ng/ml at the time of the last assessment.
- The mean cardiac MRI T2* at the time of assessment was 23.37 ms.
- And at the year of last assessment (2022).Total 52 out of 70 patients had MRI T2* value > 20 ms.
- The mean LIC was 5.18 mg/g dry weight of the liver at the time of assessment.
- And at the year of last assessment (2022).Total 23 out of 69 patients had LIC 7-15 mg/g dry weight.

IRON CHELATION THERAPY AND DOSES:

- Combination of deferasirox and deferiprone in 35 patients (23.6%) and deferasirox and deferoxamine in 10 (6.8%) patients.
- All three iron chelators were being used in 1.4% of patients.
- The mean dose of deferasirox was 32.0 mg/kg/day duration of exposure was 56.39 months.
- The mean dose for Deferoxamine was 34.42 mg/kg/d with an average duration of exposure of 40.25 months.
- The mean dose for Deferiprone is 76 mg/kg/d and the average duration of exposure of 53.86 months.
- The mean dose of Deferasirox as a single agent is more (39.45 mg/kg/day) as compared to (28.78 mg/kg/day) when used in a combination.

ADVERSE EFFECTS:

The most common adverse effect seen was GI disturbance followed by nausea and vomiting Neutropenia and thrombocytopenia are caused in patients primarily on the combination of deferasirox and deferiprone.

Rise in creatinine and transaminases are caused maximum in patients on deferasirox and deferoxamine.

Permanent with-drawl of the drug was required in only 4 patients but the remaining 84 patients continued with the iron chelation.

HOW OUR STUDY IS DIFFERENT:

The current study provides the basis for the outcome and future treatment lines of thalassemia patients. There are very few studies comparing the efficacy and safety of iron chelators in Indian children receiving regular transfusions and iron chelation therapy. Our study is one of the few studies to analyze the impact of the outcome of different iron chelators as monotherapyand in combination, their long-term effects on the growth, iron overload in vitals organs and overall quality of life of thalassemia patients.

BIBLIOGRAPHY

1. Borgna-Pignatti C, Marsella M. Iron chelation in thalassemia major. Clinical therapeutics. 2015;37:2866-77.
2. Rachmilewitz EA, Giardina PJ. How I treat thalassemia. Blood, The Journal of the American Society of Hematology. 2011;118:3479-88.
3. Aggarwal R, Prakash A, Aggarwal M. Thalassemia: an overview. Journal of the scientific society. 2014;41:3-6.
4. Rasel M, Hashmi MF, Mahboobi SK. Transfusion Iron Overload. 2024. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.
5. Coates TD. Iron overload in transfusion-dependent patients. Hematology 2014, the American Society of Hematology Education Program Book. 2019;2019:337-44.
6. Glickstein H, El RB, Link G, Breuer W, Konijn AM, Hershko C, et al. Action of chelators in iron-loaded cardiac cells: accessibility to intracellular labile iron and functional consequences. Blood. 2006;108:3195-203.
7. Dhanya R, Sedai A, Ankita K, Parmar L, Agarwal RK, Hegde S, et al. Life expectancy and risk factors for early death in patients with severe thalassemia syndromes in South India. Blood advances. 2020;4:1448-57.
8. Salimi Z, Afsharinasab M, Rostami M, Milasi YE, Ezmareh SF, Sakhaei F, et al. Iron chelators: as therapeutic agents in diseases. Annals of Medicine and Surgery. 2024;86:2759-76.
9. Ansari-Moghaddam A, Adineh HA, Zareban I, Mohammadi M, Maghsoodlu M. The survival rate of patients with beta-thalassemia major and intermedia and its trends in recent years in Iran. Epidemiology and health. 2018;40.
10. Hider RC, Zhou TA. The design of orally active iron chelators. Annals of the New York Academy of Sciences. 2005;1054:141-54.

11. Link G, Konijn AM, Breuer W, Cabantchik ZI, Hershko C. Exploring the “iron shuttle” hypothesis in chelation therapy: effects of combined deferoxamine and deferiprone treatment in hypertransfused rats with labeled iron stores and in iron-loaded rat heart cells in culture. Journal of Laboratory and Clinical Medicine. 2001;138:130-8
12. Mohd Ibrahim H, Afifah H, Elizabeth G. Clinical Practical Guidelines Manage ment of Transfusion Dependent Thalassaemia. Malaysia. 2009.
13. Chang HH, Lu MY, Peng SS, Yang YL, Lin DT, Jou ST, Lin KH. The long-term efficacy and tolerability of oral deferasirox for patients with transfusion-dependent β-thalassemia in Taiwan. Annals of hematology. 2015;94:1945-52.
14. Pepe A, Meloni A, Capra M, Cianciulli P, Prossomariti L, Malaventura C, et al. Deferasirox, deferiprone and desferrioxamine treatment in thalassemia major patients: cardiac iron and function comparison determined by quantitative magnetic resonance imaging. haematologica. 2011;96:41.
15. Taher A, Sheikh-Taha M, Sharara A, Inati A, Koussa S, et al Safety and effectiveness of 100 mg/kg/day deferiprone in patients with thalassemia major: a two-year study. Acta haematologica. 2005;114:146-9.
16. Piga A, Galanello R, Forni GL, Cappellini MD, Origa R, Zappu A, et al. Randomized phase II trial of deferasirox (Exjade, ICL670), a once-daily, orally-administered iron chelator, in comparison to deferoxamine in thalassemia patients with transfusional iron overload. haematologica. 2006;91:873-80.
17. Shah NR. Advances in iron chelation therapy: transitioning to a new oral formulation. Drugs Context. 2017;6:212502.
18. Mohanty D, Colah RB, Gorakshakar AC, Patel RZ, Master DC, Mahanta J. Prevalence of β-thalassemia and other hemoglobinopathies in six cities in India: a multicentre study. Journal of Community Genetics. 2013;4:33-42.

19. Hoffbrand AV, Taher A, Cappellini MD. How I treat transfusional iron overload. Blood, The Journal of the American Society of Hematology. 2012;120:3657-69.
20. Shah R, Trehan A, Das R, Marwaha RK. Serum ferritin in thalassemia intermedia. Indian Journal of Hematology and Blood Transfusion. 2014;30:281-5.
21. Cohen AR, Glimm E, Porter JB. Effect of transfusional iron intake on response to chelation therapy in β-thalassemia major. Blood, The Journal of the American Society of Hematology. 2008;111:583-7.
22. Schwartz E. Thalassemia syndromes. In: Miller D, Baehner R, eds. Smith's Blood Diseases of Infancy and Childhood (6th ed). St Louis, MO: Mosby; 1989:28.
23. Saliba AN, Harb AR, Taher AT. Iron chelation therapy in transfusion-dependent thalassemia patients: current strategies and future directions. J Blood Med. 2015;6:197-209.
24. Glickstein H, El RB, Link G, Breuer W, Konijn AM, Hershko C, ey al. Action of chelators in iron-loaded cardiac cells: accessibility to intracellular labile iron and functional consequences. Blood. 2006;108:3195-203.
25. Cohen AR, Glimm E, Porter JB. Effect of transfusional iron intake on response to chelation therapy in β-thalassemia major. Blood, The Journal of the American Society of Hematology. 2008;111:583-7.
26. Berdoukas V, Wood J. In search of the optimal iron chelation therapy for patients with thalassemia major. Haematologica. 2011;96:5.
27. Cappellini MD, Cohen A, Piga A, Bejaoui M, Perrotta S, Agaoglu L, et al. A phase 3 study of deferasirox (ICL670), a once-daily oral iron chelator, in patients with β-thalassemia. Blood. 2006;107:3455-62.
28. Farmaki K, Tzoumari I, Pappa C, Chouliaras G, Berdoukas V. Normalisation of total body iron load with very intensive combined chelation reverses cardiac and endocrine

complications of thalassaemia major. British journal of haematology. 2010;148:466-75.
29. Mourad FH, Hoffbrand AV, Sheikh-Taha M, Koussa S, Khoriaty AI, et al. Comparison between desferrioxamine and combined therapy with desferrioxamine and deferiprone in iron overloaded thalassaemia patients. Br J Haematol. 2003;121:187-9.
30. Al-Moshary M, Imtiaz N, Al-Mussaed E, Khan A, Ahmad S, Albqami S. Clinical and Biochemical Assessment of Liver Function Test and Its Correlation with Serum Ferritin Levels in Transfusion-dependent Thalassemia Patients. Cureus. 2020;12:e7574.
31. Sidhu S, Kakkar S, Dewan P, Bansal N, Sobti PC. Adherence to iron chelation therapy and its determinants. International Journal of Hematology-Oncology and Stem Cell Research. 2021;15:27-34.
32. Parakh N, Chandra J. Correlation of transient elastography with mri t2* and serum ferritin levels in children with transfusion-dependent thalassemia. Indian Pediatrics. 2022;59:929-32.
33. Mohamed YA, Morgan DS, Hussein AM, Mohamed AA. Noninvasive assessment and risk factors of liver fibrosis in pediatric patients with beta thalassemia major using transient elastography. Beni-Suef University Journal of Basic and Applied Sciences. 2022;11:134.
34. Maurer HS, Lloyd-Still JD, Ingrisano C, Gonzalez-Crussi F, Honig GR. A prospective evaluation of iron chelation therapy in children with severe β-thalassemia: a six-year study. American Journal of Diseases of Children. 1988;142:287-92.
35. Palit S, Bhuiyan RH, Aklima J, Emran TB, Dash R. A study of the prevalence of thalassemia and its correlation with liver function test in different age and sex group in the Chittagong district of Bangladesh. Journal of basic and clinical pharmacy. 2012;3:352.
36. Brittenham GM, Griffith PM, Nienhuis AW, McLaren CE, Young NS, Tucker EE, et al. Efficacy of deferoxamine in preventing

complications of iron overload in patients with thalassemia major. New England Journal of Medicine. 1994;331:567-73.
37. Daar S, Pathare AV. Combined therapy with desferrioxamine and deferiprone in beta thalassemia major patients with transfusional iron overload. Annals of hematology. 2006;85:315-9.
38. Jin LW, Tahir NA, Islahudin F, Chuen LS. Adherence and Health-related Quality of Life of Transfusion-Dependent Thalassemia Patients. Archives of Pharmacy Practice. 2023;14:89-95.
39. Vichinsky EP. Changing patterns of thalassemia worldwide. Annals of the New York Academy of Sciences. 2005;1054:18-24.
40. Marengo-Rowe AJ. The thalassemias and related disorders. Proc (Bayl Univ Med Cent). 2007;20:27-31.
41. Entezari S, Haghi SM, Norouzkhani N, Sahebnazar B, Vosoughian F, Akbarzadeh D, et al. Iron Chelators in Treatment of Iron overload. J Toxicol. 2022;2022:4911205.
42. Taher A, El‐Beshlawy A, Elalfy MS, Al Zir K, Daar S, Habr D, et al. Efficacy and safety of deferasirox, an oral iron chelator, in heavily iron‐overloaded patients with beta-thalassemia: The ESCALATOR study. Eur J Haematol. 2009;82:458-6
43. Gomber S, Jain P, Sharma S, Narang M. Comparative efficacy and safety of oral iron chelators and their novel combination in children with thalassemia. Indian Pediatr. 2016;53:207–10.
44. Cassinerio E, Roghi A, Pedrotti P, Brevi F, Zanaboni L, Graziadei G, et al. Cardiac iron removal and functional cardiac improvement by different iron chelation regimens in thalassemia major patients. Ann Hematol. 2012;91:1443- 9.
45. Cappellini MD, Cohen A, Piga A, Bejaoui M, Perrotta S, Agaoglu L, et al. A phase 3 study of deferasirox (ICL670), a once-daily oral iron chelator, in patients with β-thalassemia. Blood. 2006;107:3455-62.
46. Xia S, Zhang W, Huang L, Jiang H. Comparative efficacy and safety of deferoxamine, deferiprone and deferasirox on severe

thalassemia: a meta-analysis of 16 randomized controlled trials. PLoS One. 2013;8:e82662.

47. Lal A, Porter J, Sweeters N, Ng V, Evans P, Neumayr L, et al. Combined chelation therapy with deferasirox and deferoxamine in thalassemia. Blood Cells Mol Dis. 2013;50:99-104.
48. Farmaki K, Tzoumari I, Pappa C. Oral chelators in transfusion-dependent thalassemia major patients may prevent or reverse iron overload complications. Blood Cells Mol Dis. 2011;47:33-40.
49. Chang HH, Lu MY, Liao YM, Lin PC, Yang YL, Lin DT, et al. Improved efficacy and tolerability of oral deferasirox by twice-daily dosing for patients with transfusion-dependent βthalassemia. Pediatr Blood Cancer. 2011;56:420-4.
50. Tanner MA, Galanello R, Dessi C, Smith GC, Westwood MA, Agus A, et al. Combined chelation therapy in thalassemia major for the treatment of severe myocardial siderosis with left ventricular dysfunction. J Cardiovasc Magn Reson. 2008;10:12.
51. Karami H, Kosaryan M, Amree AH, Darvishi-Khezri H, Mousavi M. Combination Iron Chelation Therapy with Deferiprone and Deferasirox in Iron-Overloaded Patients with Transfusion-Dependent β-Thalassemia Major. Clin Pract. 2017;7:912.
52. Totadri S, Bansal D, Bhatia P, Attri SV, Trehan A, Marwaha RK. The deferiprone and deferasirox combination is efficacious in iron overloaded patients with β-thalassemia major: A prospective, single center, open-label study. Pediatr Blood Cancer. 2015;62:1592-6.

53. Ejaz MS, Baloch S, Arif F. Efficacy and adverse effects of oral chelating therapy (deferasirox) in multi-transfused Pakistani children with β-thalassemia major. Pakistan Journal of Medical Sciences. 2015;31:621.
54. Nuzzi R, Geronazzo G, Tridico F, Nuzzi A, Caselgrandi P, Piga AG. Long-term effects of Iron chelating agents on ocular function in patients with thalassemia major. Clinical Ophthalmology. 2021;20:2099-109.
55. Sarbay H, Kara MA. Proteinuria due to increased dose of deferasirox in a pediatric patient with thalassemia major: case report. Int J Contemp Pediatr. 2018;5:2338-40.
56. Lee WJ, Mohd Tahir NA, Chun GY, Li SC. The impact of chelation compliance in health outcome and health-related quality of life in thalassemia patients: a systematic review. Health and Quality of Life Outcomes. 2024;22:14.
57. Mokhtar GM, Gadallah M, El Sherif NH, Ali HT. Morbidities and mortality in Transfusion-Dependent Beta-Thalassemia patients (single-Center experience). Pediatr Hematol Oncol. 2013;30:93-103.
58. Sukhmani S, Shruti K, Priyanka D, Namita B, Praveen S. Adherence to Iron Chelation Therapy and its determinants. Int J Hematology-Oncology Stem Cell Res. 2021;15:27-34.

KEY TO MASTER CHART

U – Urban

R – Rural

Weight interpretation : <3rd centile – 0

3-97th centile – 1- 2

>97th centile – 3

Height interpretation: <3rd centile – 0

3-97th centile – 1- 2

>97th centile – 3

BMI interpretation: Normal- 0

Overweight – 1

Obese – 2

Socioeconomic scale (SES): Upper class – 1

Upper middle class- 2

Lower middle class- 3

Upper lower class -4

Lower class – 5

Y- YES

N- NO

Y0 to Y16 – 2022 to 2007

Mean Hemoglobin (gm/dl) : <7 – 1

7-9 -2

9-10.5 – 3

>10.5 – 4

SF – serum ferritin

SF0 (year) – 2022

SF16 (year) – 2007

Table 1

Tanner Stage	Breasts	Pubic Hair	Growth	Other
1	Elevation of papilla only	Villus hair only	2-2.4 inches per year	Adrenarche and ovarian growth
2	Breast bud under the areola, areola enlargement	Sparse hair along the labia	2.8-3.2 inches per year	Clitoral enlargement, labia pigmentation, growth of uterus
3	Breast tissue grows but has no contour or separation	Coarser hair curled pigmented covers the pubes	3.2 inches per year	Axillary hair, acne
4	Projection of areola and papilla, secondary mound formation	Adult hair, does not spread to the thigh	2.8 inches per year	Menarche and development of menses
5	Adult-type contour, projection of papilla only	Adult hair, spreads to the medial thigh	Cessation of linear growth	Adult genitalia

Table 2

Tanner Stage	Genitalia	Pubic Hair	Growth	Other
1	Testes <2.5 cm	Villus hair only	2.0-2.4 inches per year	Adrenarche
2	Testes 2.5-3.2 cm Thinning and reddening of the scrotum	Sparse hair at penis base	2.0-2.4 inches per year	Decreases in body fat
3	Testes 3.3-4.0 cm Increase of penis length	Thicker curly hair spreads to the pubis	2.8-3.2 inches per year	Gynecomastia, voice break, increased muscle mass
4	Testes 4.1-4.5 cm, penis growth darkening of scrotum	Adult hair does not spread to thighs	4.0 inches per year	Axillary hair, voice change, acne
5	Testes >4.5cm, adult genitalia	Adult hair spreads to medial thigh	Deceleration, cessation	Facial hair, muscle mass increases

PARAMETERS OF SAFETY (ADVERSE EFFECT GRADING ACCORDING TO CTCAE VER 5)

CTCAE TERM	GRADE 1	GRADE 2	GRADE 3	GRADE 4	GRADE 5
1. RASH	Mild often resolve spontaneously	Moderate often resolve spontaneously and continue treatment without dose adjustment	Severe Rash Interrupt treatment and consider the use of systemic corticoids	-	-
2. PAIN ABDOMEN *Definition*: A disorder characterized by a sensation of marked discomfort in the abdominal region.	Mild pain	Moderate pain; limiting instrumental ADL	Severe pain; limiting self careADL	-	-
3. NAUSEA *Definition*: A disorder characterized by a queasy sensation and/or the urge to vomit.	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition	Inadequate oral caloric or fluid intake; tube feeding, TPN, or hospitalization indicated	-	-
4. VOMITING *Definition*: A disorder characterized by the reflexive act of ejecting the contents of the stomach through the mouth	Intervention not indicated	Outpatient IV hydration; medical intervention indicated	Tube feeding, TPN, or hospitalization indicated	Life-threatening consequences	Death
5. NEUTROPENIA	-	-	ANC <1000/ µl	Life threating consequences urgent intervention indicated	Death
6. THROMBOCYTOPENIA	< LLN – 75000/µl	50000 – 75000/µl	< 25000 – 50000/µl	< 25000/µl	
7. RISE IN SERUM CREATININE	-	-	-	-	-
8. Raised AST/ALT	> 1.5 - 5 ULN	> 5 - 10 ULN	> 10 ULN	-	-
9. VISUAL DEFECTS	-	-	-	-	-
10. AUDITORY DEFECTS	-	-	-	-	-

S.No	Name	DOB	AGE AT ASSESSMENT (MONTHS)	AGE (YEARS)	Sex	Locality	A+	A-	B+	B-	AB+	AB-	O+	O-	weight (actual)	weight (expected)	Weight (interpretation)	Height (actual) CM	Height (expected)	Height (interpretation)	BMI (actual)	BMI (Expected)	BMI (interpretation)	Anti Hbs	anti HCV	HCV- RNA	HIV	HbsAg	Hb F (FATHER)
1	A	20/11/2010	144	12.0	M	U			Y						42	44	2	145	149	1	20.33	20	2	positive	negative	negative	negative	negative	0.4
2	SA	09-05-2010	72	13.0	M	U							Y		28	29	0	138	140	0	14.7	15	0	positive	negative	negative	negative	negative	1
3	RK	17/7/2015	36	9.0	F	U					Y				22	21	2	121	119	2	15	14	2	positive	negative	negative	negative	negative	0.7
4	A	20/12/2008	78	15.0	M	U	Y								36	38	0	146	148	0	16.9	17	0	positive	negative	negative	negative	negative	1.2
5	A	28/7/2016	84	7.0	M	R			Y						22	24	2	124	126	2	14.3	15	2	positive	negative	negative	negative	negative	0.6
6	AS	19/01/2012	132	11.0	M	U				Y					32	35	2	143	145	2	15.6	16	1	positive	negative	negative	negative	negative	0.4
7	A	23/09/2011	132	11.0	M	U					Y				28	30	0	137	140	0	14.9	15	0	positive	negative	negative	negative	negative	
8	A	18/12/2017	66	5.5	F	U			Y						11	10	0	91	90	0	13.3	13	1	positive	negative	negative	negative	negative	
9	AM	10-10-2020	36	3.0	M	R							Y		13	15	2	95	100	2	14.4	15	0	positive	negative	negative	negative	negative	0.8
10	AR	02-07-2017	20	7.0	M	U	Y								19	18	2	116	115	2	14.1	14	0	positive	negative	negative	negative	negative	92
11	GK	10-05-2005	144	12.0	F	U			Y						36	39	0	152	155	1	15.6	16	0	positive	negative	negative	negative	negative	
12	V	17/11/2005	18	1.5	M	R			Y						52	55	0	164	168	0	19.3	20	2	positive	negative	negative	negative	negative	0.7
13	RS	31/1/2007	192	16.0	M	R					Y				33	36	0	157	160	0	13.4	14	0	positive	positive	negative	negative	negative	1.6
14	IP	21/12/2007	192	16.0	F	U							Y		55	59	2	154	158	2	23.2	24	2	positive	negative	negative	negative	negative	
15	GS	19/10/2009	168	14.0	M	U							Y		35	38	0	148	146	1	16	16.1	1	positive	negative	negative	negative	negative	1.4
16	MB	03-05-2012	132	11.0	M	U	Y								19	22	0	120	124	0	13.2	14	0	positive	positive	positive	negative	negative	
17	KS	29/5/2009	168	14.0	M	R			Y						30	27	0	144	140	0	14.5	14	0	positive	negative	negative	negative	negative	0
18	MS	24/4/13	120	10.0	M	U	Y								19	20	0	121	122	0	13	13	0	positive	positive	positive	negative	negative	
19	MS	31/1/2008	180	15.0	M	U	Y								26	24	0	135	132	0	14.3	14	0	positive	positive	positive	negative	negative	
20	V	11-01-2017	72	6.0	M	U							Y		16	15	2	106	104	3	14.2	14	0	positive	negative	negative	negative	negative	
21	HK	08-03-2015	78	6.5	M	U			Y						23	26	2	125	129	2	14.7	15	1	positive	negative	negative	negative	negative	0.6
22	DC	08-12-2019	48	4.0	M	U	Y								13	15	0	98	100	2	13.5	14	0	positive	negative	negative	negative	negative	0
23	VK	03-09-2016	84	7.0	M	R			Y						21	20	2	122	120	2	14.1	14	1	positive	negative	negative	negative	negative	
24	S	01-12-2008	180	15.0	M	U							Y		27	30	0	140	143	0	13.8	14	0	positive	negative	negative	negative	negative	5.8
25	R	15/2/2009	168	14.0	F	U			Y						39	38	1	143	141	0	19.1	19	2	positive	negative	negative	negative	negative	0.7
26	JK	10-04-2017	72	6.0	F	U								Y	16	14	1	109	105	2	13.5	13	0	positive	negative	negative	negative	negative	
27	RK	07-05-2011	144	12.0	M	U					Y				26	29	0	129	134	0	15.6	16	2	positive	positive	positive	positive	negative	
28	BK	02-10-2019	48	4.0	F	U			Y						14	16	1	104	107	3	12.9	13	0	positive	negative	negative	negative	negative	0.3
29	S	01-08-2012	17	1.4	M	U							Y		22	25	0	133	137	0	12.4	13	0	positive	negative	negative	negative	negative	1
30	GK	12-06-2014	18	1.5	F	R							Y		28	30	0	119	121	2	19.8	20	2	positive	negative	negative	negative	negative	1
31	MT	14/09/2013	12	1.0	M	U							Y		23	26	2	122	125	1	15.5	16	2	positive	negative	negative	negative	negative	5.4
32	AA	02-07-2008	6	0.5	M	R							Y		44	46	0	163	166	2	16.6	17	1	positive	negative	negative	negative	negative	1
33	SS	01-09-2011	6	0.5	M	R					Y				22	20	0	138	135	0	11.6	11	0	positive	negative	negative	negative	negative	1
34	AK	10-02-2018	18	1.5	F	R								Y	16	19	2	102	106	2	15.4	16	2	positive	negative	negative	negative	negative	0.8
35	DJ	03-10-2020	48	4.0	F	U							Y		14	18	2	104	108	2	12.9	13	0	positive	negative	negative	negative	negative	0.8
36	HS	19/11/11	144	12.0	M	U							Y		43	40	2	150	148	3	19.1	19	2	positive	negative	negative	negative	negative	
37	N	05-08-2020	33	2.8	F	R							Y		16	18	3	97	100	2	17	17.2	2	positive	negative	negative	negative	negative	
38	K	13/8/2012	132	11.0	F	U							Y		22	25	0	14.8	15	0	14.8	15	1	positive	negative	negative	negative	negative	0.5
39	K	13/11/2019	36	3.0	M	R			Y						13	12	1	96	95	2	14.1	14	2	positive	negative	negative	negative	negative	1
40	P	18/11/2007	186	15.5	M	U							Y		39	38	1	151	149	2	17.1	17	1	positive	negative	negative	negative	negative	
41	PS	10-09-2010	144	12.0	M	R							Y		38	41	1	153	155	2	16.2	16.4	1	positive	negative	negative	negative	negative	1.6
42	K	13/6/2007	192	16.0	M	U			Y						30	34	0	145	148	0	14.3	14.5	0	positive	negative	negative	negative	negative	
43	K	22/01/2016	84	7.0	M	U			Y						17	15	1	114	112	2	13.1	13	0	positive	negative	negative	negative	negative	
44	AKB	08-09-2006	204	17.0	M	U				Y					44	47	3	161	163	2	17	17.1	0	positive	negative	negative	negative	negative	1
45	R2	20/3/2014	108	9.0	F	U							Y		33	36	3	131	135	2	19.2	19.5	2	positive	negative	negative	negative	negative	
46	KS	29/11/2014	108	9.0	M	U				Y					28	31	2	126	130	2	17.6	18	2	positive	negative	negative	negative	negative	0.4
47	NA	20/9/2014	108	9.0	F	U							Y		23	25	2	120	123	1	16	16.2	2	positive	negative	negative	negative	negative	
48	GK	09-07-2016	78	6.5	F	U					Y				19	22	3	117	120	2	13.9	14	1	positive	negative	negative	negative	negative	1.5
49	GK	16/12/12	137	11.4	F	U			Y						27	30	1	134	138	2	15	15.2	1	positive	negative	negative	negative	negative	
50	M	14/11/2006	204	17.0	M	U			Y						58	61	2	163	166	1	21.8	22	2	positive	negative	negative	negative	negative	0.6
51	BS	17/12/2018	56	4.7	M	R			Y						15	17	2	100	103	2	15	15.2	1	positive	negative	negative	negative	negative	
52	K	12-06-2017	72	6.0	F	U			Y						19	17	2	111	108	3	15.4	15	2	positive	negative	negative	negative	negative	
53	G	26/11/2017	70	5.8	M	U							Y		18	20	2	113	116	2	14.1	14.3	0	positive	negative	negative	negative	negative	
54	NV	01-12-2008	180	15.0	M	U	Y								40	44	0	147	151	0	18.5	18.9	2	positive	positive	negative	negative	negative	0.3
55	DG	25/9/2010	156	13.0	M	U							Y		47	50	3	147	151	2	21.8	22	2	positive	negative	negative	negative	negative	0.5
56	D	02-07-2008	180	15.0	F	U							Y		44	48	1	163	169	2	16.6	17	1	positive	negative	negative	negative	negative	1
57	R	07-07-2016	72	6.0	F	U							Y		15	18	0	100	104	0	15	15.2	2	positive	negative	negative	negative	negative	0.9
58	R	07-05-2011	108	9.0	M	U					Y				26	30	0	129	133	0	15.6	16	1	positive	negative	negative	negative	negative	
59	K	15/10/2010	156	13.0	F	U			Y						41	43	2	145	147	1	19.5	19.8	2	positive	negative	negative	negative	negative	1
60	AC	27/8/2005	210	17.5	M	U			Y						47	50	0	163	166	0	17.7	18	0	positive	negative	negative	negative	negative	0.8
61	K	07-04-2016	78	6.5	M	U							Y		21	20	2	122	120	2	14.1	14	0	positive	negative	negative	negative	negative	94.2
62	KS	24/01/2006	210	17.5	M	R	Y								50	54	0	155	158	0	20.8	21	2	positive	negative	negative	negative	negative	
63	P	31/10/2006	204	17.0	M	U							Y		31	30	0	148	145	0	14.2	14	0	positive	negative	negative	positive	negative	3.4
64	A	23/05/2005	204	17.0	M	U							Y		53	50	1	162	160	2	20.2	20	2	positive	negative	negative	negative	negative	0.5
65	GS	19/10/2009	132	11.0	M	U							Y		35	39	0	148	151	1	16	16.2	1	positive	negative	negative	negative	negative	1.4
66	A	02-10-2015	96	8.0	F	U			Y						24	20	2	125	121	1	15.4	15	2	positive	negative	negative	negative	negative	
67	MK	14/11/13	108	9.0	F	R				Y					24	28	1	131	134	2	14	14.3	0	positive	negative	negative	negative	negative	
68	Ak	25/05/2010	156	13.0	F	R						Y			34	38	1	144	147	1	16.4	16.7	1	positive	negative	negative	negative	negative	5.3
69	A	19/10/2009	156	13.0	M	R			Y						37	40	1	147	150	0	17.1	17.4	1	positive	negative	negative	negative	negative	
70	S	08-04-2013	113	9.4	F	U	Y								36	35	2	145	143	3	17.1	17	2	positive	negative	negative	negative	negative	0.8
71	Dv	01-03-2006	204	17.0	M	U							Y		58	61	2	169	172	2	20.3	20.7	2	positive	negative	negative	negative	negative	0
72	HS	28/8/2020	36	3.0	M	U	Y								11	14	0	93	97	2	12.7	13	0	positive	negative	negative	negative	negative	1
73	A	21/9/2008	168	14.0	F	U							Y		42	45	2	144	148	0	20.3	20.6	2	positive	negative	negative	negative	negative	1.5
74	A	27/10/2008	168	14.0	F	U							Y		47	50	2	147	151	0	21.8	22	2	positive	positive	negative	negative	negative	0.3

S.No	HbA1 (Father)	Hb F (mother)	HbA1 (Mother)	MODIFIED KUPPUSWAMY SCALE	SES	AGE AT ENROLLMENT IN MONTHS	AGE AT DIAGNOSIS	date of assessment	AGE AT START OF CHELATION	COMPLIANCE	SPLENECTOMY	MENINGOCOCCAL VACCINE	PNEUMOCOCCAL VACCINE	formula for iron overload	annual transfusion requirement (Y0)-2022	transfusion_Y1	transfusion_Y2	transfusion_Y3	transfusion_Y4
1	5.6	1.3	5.9	10	4	24	24	03-01-2013	28	Y	N	N	N	0.3		174	204	101	226
2	5	1	25.8	18	2	72	8	07-12-2018	96	Y	N	N	N	0.48		273	294	266.5	275
3	8.9	5.2	98.3	16	2	40	12	27/5/2019	40	Y	N	N	N	0.41	231	303	334	137	363
4	5.3	1.2	5.3	12	3	84	6	20/5/2015	84	Y	N	N	N	0.36	208	202	223.5	208	212
5	5.8	1.8	4.4	14	3	60	4.9	05-05-2021	60	Y	N	N	N	0.45	255	237			
6	4.6	1	5.7	12	3	48	7	16/8/2014	48	Y	N	N	N	0.45	254	260	224.5	282	273.3
7				16	2	132	8	18/1/2022	132	Y	N	N	N	0.41	236	60			
8				18	2	48	10	03-07-2022	60	Y	N	N	N	0.39	220				
9	5.7	3.6	5.8	10	4	21	9	07-09-2022	21	Y	N	N	N	0.44	252				
10		26		16	2	31	12	26/9/19	31	Y	N	N	N	0.43	246	298	204	249	
11				12	3	144	23	31/8/19	156	Y	N	N	N	0.35	200	212	145	302	
12	5.8	0.4	5.6	16	2	18	14	15/11/13	96	Y	N	N	N	0.1		50	207		331
13	7.1	0.6	6.4	12	3	12	8	12-01-2015	96	N	N	N	N	0.53	304	306	220	206	356
14				10	4	24	16	29/10/11	48	Y	N	N	N	0.31	179	117	171	173	180
15	4.4	1	5.3	16	2	4	4	23/7/11	24	Y	N	N	N	0.32	184				
16				14	3	84	14	18/12/19	84	Y	N	N	N	0.5	287	346	195		
17	5.1	0	5.3	12	3	11	11	04-03-2012	36	N	N	N	N	0.43	244	247	195	271	195
18				18	2	72	9	28/9/19	72	Y	N	N	N	0.53	301	326	269		
19				12	3	132	5	28/9/19	138	Y	N	N	N	0.48	272	317	255		
20				16	2	6	6	30/9/19	10	Y	N	N	N	0.51	288	294	193	195	235
21	6.4	0.5	4.6	10	4	24	8	09-10-2018	36	Y	N	N	N	0.53	303	318	179	290	292
22	4.7	0.4	4.4	16	2	33	7	17/5/22	33	Y	N	N	N	0.36	208				
23				12	3	16	11	20/10/18	31	Y	N	N	N	0.38	216	277	178	228	177
24			5	10	4	108	18	31/10/17	113	Y	N	N	N	0.58	328	206	246	442	372
25	6.8	0.6	6.4	10	4	14	9	14/1/13	48	N	N	N	N	0.31	175	152	225	201	290
26				16	2	9	8	19/9/18	12	Y	N	N	N	0.48	275	260	255	226	181
27				12	3	108	12	31/3/20	96	Y	N	N	N	0.47	270	314	261		
28	6.2	0.9	4.9	14	3	16	11	10-09-2020	20	Y	N	N	N	0.35	202	196	153		
29	5	1	5	10	4	17	8	03-10-2014	26	Y	N	N	N	0.45	255	319	199	266	238
30	5	0.4	4.5	10	4	18	5.6	12-08-2016	24	Y	N	N	N	0.4	226	231	176	224	249
31	94.6	6.3	93.7	12	3	12	6	24/06/15	24	Y	N	N	N	0.53	300	292	210	293	262
32		1	5.8	14	3	13	7.2	01-06-2011	36	Y	N	N	N	0.39	220	235	176	190	184
33	5.3	1	5.3	12	3	6	5	04-10-2013	27	Y	N	N	N	0.46	262	289	217	215	287
34	4.1	0.8	6.5	16	2	18	6	13/2/21	28	Y	N	N	N	0.49	285	256	108		
35	6	0.8	5.6	14	3	15	11	12-07-2020	24	Y	N	N	N	0.42	239	216	222		
36				10	4	144	6	01-05-2023	144	Y	N	N	N	0.37	210				
37				16	2	5	4.9	21/7/21	14	N	N	N	N	0.42	240	208	107		
38	5.6	0.8	5.6	16	2	71	4.8	29/6/19	65	N	N	N	N	0.4	227	231	186	162	
39	6.6	1.1	6.1	12	3	10	5	06-12-2021	24	Y	N	N	N	0.39	220	223			
40		0.6	5.6	16	2	14	8	21/8/10	36	Y	N	N	N	0.4	230	282	198	229	226
41	5.3	1	5.6	12	3	8	6	19/7/13	36	N	N	N	N	0.47	265	292	191	245	261
42				14	3	156	7	31/8/22	156	Y	N	N	N	0.25	142				
43				10	4	72	3.6	10-07-2022	72	Y	N	N	N	0.16	92				
44	6.3	0.8	6.8	12	3	18	5.3	19/10/09	36	Y	N	N	N	0.42	245	259	182	182	272
45				12	3	65	4.8	29/01/20	72	Y	N	N	N	0.42	238	183	222		
46	5.1	0.6	3.3	10	4	11	7	16/10/19	60	Y	N	N	N	0.42	240	295	203	260	249
47				20	1	78	5	31/3/21	78	Y	N	N	N	0.43	245	238			
48	5.9	1.4	5.5	18	2	36	7	11-07-2019	36	Y	N	N	N	0.52	298	315	267		
49				22	2	84	8.3	19/9/20	96	Y	N	N	N	0.41		234	167	176	
50	6.6	0.4	6.3	10	4	5	7.9	07-06-2009	36	Y	N	N	N	0.32	185	201	176	224	237
51				10	4	42	6.7	27/11/22	48	Y	N	N	N	0.35	200	204	189	194	202
52				14	3	36	8.8	25/12/20	36	N	N	N	N	0.46	263	296	145		
53				10	4	9	5	04-08-2019	17	N	N	N	N	0.54	305	295	196	242	
54	8.5	0.6	4.8	12	3	84	6	17/4/15	87	Y	N	N	N	0.38	216	214	175	247	269
55	4.8	0.8	4.7	16	2	15	6.7	02-04-2013	30	Y	N	N	N	0.3	170	175	149	222	246
56	5.9	1	5.8	10	4	6	6.3	04-08-2019	132	N	N	N	N	0.39	220	235	176	190	184
57	5.6	1.1	6.1	10	4	72	7.4	17/3/23	72	Y	N	N	N	0.45	254	260	224.5	282	273.3
58				10	4	108	8	31/3/20	108	Y	N	N	N	0.47	270	314	133		
59	5.4	1	5.8	10	4	6	6.9	04-12-2018	84	Y	N	N	N	0.35	200	240	199	275	242
60	5.8	0.4	5.3	12	3	24	8	15/8/09	48	Y	N	N	N	0.29	167	180	116	167	207
61	5.2	1	5.4	20	2	6	7.4	28/8/18	24	N	N	N	N	0.39	224	249	185	302	215
62				12	3	10	6	08-06-2008	31	Y	N	N	N	0.33	190	229	74.6	172	239
63	1.7	3.7	3.7	14	3	9	6.2	15/01/13	84	Y	N	N	N	0.47	269	323	197	250	266
64	4.8	1.7	6	16	2	156	8.9	04-03-2019	161	Y	N	N	N	0.41	236	283	186	237	
65	4.4	1	5.3	12	3	6	10	25/7/11	20	N	N	N	N	0.32	184				
66				12	3	72	14	18/1/22	72	Y	N	N	N	0.44	248	65.7			
67		0.7	6.6	10	4	48	20	09-10-2019	60	Y	N	N	N	0.47	266	278	260	264	223
68	5.3	1	5	12	3	108	11	28/8/19	108	Y	N	N	N	0.37	227		255	248	
69				12	3	60	9.4	19/5/15	72	Y	N	N	N	0.44	248	253	193	311	391
70	6.1			14	3	54	7.8	10-08-2018	60	Y	N	N	N	0.37	214	213	186	249	141
71	3.6	0	5.9	10	4	14	6.9	11-07-2009	48	Y	N	N	N	0.35	200	280	182	239	299
72	5.4	1.3	4.6	12	3	16	8	17/10/22	24	Y	N	N	N	0.3	174				
73	6.2	0.7	5.9	16	2	9	6.5	15/3/12	36	Y	N	N	N	0.3	175	190	157	191	237
74	5.4	2.5	4.8	12	3	17	5.8	17/4/12	48	Y	N	N	N	0.32	185	205	217	217	228

S.No	transfusion_Y5	transfusion_Y6	transfusion_Y7	transfusion_Y8	transfusion_Y9	transfusion_Y10	transfusion_Y11	transfusion_Y12	transfusion_Y13	transfusion_Y14	transfusion_Y15	transfusion_Y16	mean transfusion	Total transfusion	Iron over load	Hb group	Average Hb (Y0)	Y1	Y2	Y3	Y4
1	250	260	288.9	269	295	254							232.1	2321.9	2506.68	4	10.3	8.8	9	9	9.3
2	371	322											257.35	1801.5	1945.08	2	8.1	9	8.8	8.65	8.9
3													273.6	1368	1477.44	2	8	8.7	8.9	9.4	8.8
4	207	242	111										201.6	1613.5	1742.58	3	9.8	9.9	9.5	9.5	9.5
5													246	492	531.36	2	8.9	9	8.8		
6	234	292	256	290	165								253	2530.8	2733.264	3	9.2	9.6	9	9.4	9
7													148	296	319.68	2	7	6.1	7	7.4	6.8
8													220	220	237.6	2	8.1	9	8.8	8.7	8.9
9													252	252	272.16	2	8.7	8.8	8.9	9.2	8
10													249	997	1076.76	3	9.1	9.8	9.5	9.37	
11													214	859	927.72	1	6.4	4.4	6.2	8.6	
12	260			271	140	261	253	242	225	211	244		180	2875	3105	2	8.4	9.2	8.5	8.6	8.2
13	273	327	267	282	271	275	200	188	163				280	3638	3929.04	2	8.6	8.4	8.8	8.6	8.5
14	192	202	233	244	270	182	221						214.9	2364	2553.12	3	9	9.2	9.4	9.3	9
15			189	282	235	220	208						109.83	1318	1423.44	3	9.3				
16													276	828	894.24	4	10.6	10.7	10	10	
17	271	218	322	134	219	336	238	226	209				255.76	3325	3591	2	8.8	9	9	9.2	8.9
18													298.66	896	967.68	3	9.1	9.8	9.6	9	8.8
19													281.33	844	911.52	3	9.4	9.4	8.8	8.9	
20													241	1205	1301.4	3	9.7	12.9	9.6	9.1	10.9
21													276.4	1382	1492.56	3	9.2	9.1	8.9	8.7	9
22													208	208	224.64	3	9.8	10	10.2	9.8	9.6
23	257	72.2											200	1405.2	1517.616	3	9.2	9.5	8.7	9.8	9.8
24	193												297.83	1787	1929.96	2	8.9	8.5	8.4	8.7	9.2
25	238	278	264	272	242								233.7	2337	2523.96	3	9	9.7	9.9	9.7	9.2
26													119.7	1197	1292.76	3	9.6	10	9.7	9.6	10.8
27													281.66	845	912.6	3	9.4	9.3	9.2		
28													183.66	551	595.08	3	9	9.3	9.5		
29	269	235	257	259	70								236.7	2367	2556.36	3	9.3	10.3	9.3	9.6	9.3
30	237												223.8	1343	1450.44	3	9.1	9.7	9.1	9.4	9.4
31	238	266	242										262.87	2103	2271.24	3	9.9	9.9	9.7	9.7	9.6
32	283	253	260	268	251	214	230						251.2	2764	2985.12	2	8.6	8.4	8.5	9	8.7
33	269	265	294	230	170	192							269	2690	2905.2	4	10.3	10.1	9.7	9.4	9.6
34													216.33	649	700.92	4	10.5	10.8	10.7		
35													169.25	677	731.16	3	9.5	10.4	10.7		
36													210	210	226.8	3	9	9.2	9	8.5	9.3
37													185	555	599.4	4	10.1	10.7	10		
38													201.5	806	870.48	3	9.8	10	9.3	10	
39													221.5	443	478.44	3	9.7	9.7			
40	138	280	325	286	234	258							268.6	2686	2900.88	3	9.1	8.7	8.7	8.5	8.2
41	246	277	305	240	228	178							272.8	2728	2946.24	4	10.3	9.5	9.5	9.1	9.1
42													142	142	153.36	2	8.7	8.5	8.8	8.9	8.6
43													92	92	99.36	3	9.7	10.2	9.7	9.8	10.4
44	301	295	311	286	234	256	250	211					273.6	3284	3546.72	3	9	10.2	8.9	9	8.7
45													214.33	643	694.44	3	9.5	9.8	9.5		
46	192												239.83	1439	1554.12	4	10.2	10.2	9.6	9.8	8.9
47													241.5	483	521.64	3	9.1	9.3	9		
48													293.33	880	950.4	3	9.1	8.9	9.1	9.4	
49													192.33	577	623.16	2	8.4	7.9	8.6	9.1	
50	238	248	183	212	215	232	238	225	192	155	148		220.6	3309	3573.72	2	8.8	9.1	9.4	9.7	9.4
51	214												200.5	1203	1299.24	2	8.7	8.8	8.9	8.6	8.4
52													234.66	704	760.32	3	9.2	9.2	9.1	9.3	
53													259.5	1038	1121.04	3	9.7	10.2	8.7	9.4	
54	295	294	239										243.62	1949	2104.92	2	8.9	9.4	8.9	8.9	9
55	267	260	290	258	216								225.3	2253	2433.24	3	9.9	9.7	9.7	9.3	9.5
56	283	253	260	268	251	214	230						251.2	2764	2985.12	2	8.6	8.4	8.5	8.7	9
57	234	292											259.85	1819.8	1965.384	2	8.8	7.6	8	8.2	8.9
58													239	717	774.36	3	9.4	9.3	9.2		
59	229	255	281	282	236								243.9	2439	2634.12	3	9.2	9	9	9	9.4
60	232	241	250	266	277								210.3	2103	2271.24	3	9.7	9.7	9.6	9.5	9.5
61													235	1175	1269	3	9.3	9.1	8.7	9.3	9.7
62	198	261	265	296	261	251							243.66	2436.6	2631.528	3	9	9.4	9.5	9.1	9.1
63	250		266	247	239	225	218						250	2750	2970	2	8.8	8.5	9.4	9.1	9.4
64													235.5	942	1017.36	2	8.4	8.2	8.5	8.1	
65			189	282	235								222.5	890	961.2	2	8.3				
66													156.85	313.7	338.796	1	6.5	5.9	7	6.4	6
67													258	1291	1394.28	3	9.2	8.9	8.7	9	9.6
68													243.33	730	788.4	3	9.2	9.6	9	9.2	
69	216	425	300	360	152								284.9	2849	3076.92	2	8	8.6	8.6	8.4	7.9
70	159												193.66	1162	1254.96	2	8.7	9.6	9.3	9.8	9.6
71	245	281	286	272	244	291	270						280.8	3089	3336.12	4	9.4	9.9	9.3	9.5	9.2
72													174	174	187.92	4	10.5	11	10.4	11.2	9.9
73	220	218	285	248	229								215	2150	2322	3	9.1	9.8	9.4	9.3	9.4
74	246	225	281	217									224.55	2021	2182.68	3	9.5	9.3	8.8	9.7	8.7

S.No	Y5	Y6	Y7	Y8	Y9	Y10	Y11	Y12	Y13	Y14	Y15	Y16	Serum Ferritin levels (SF0)	SF1	SF2	SF3	SF4	SF5	SF6	SF7	SF8	SF9	SF10	SF11	SF12	SF13	SF14	SF15	TANNERS STAGE (>10 years)	DEFERASIROX (USED)	MEAN DOSE (mg/kg)	months of exposure	DEFEROXAMINE (USED)	MEAN DOSE (mg/kg)	months of exposure
1	9.1	8.9	9.5	9.5	9.1	10.4							690	644.2	779.9	714.4	980.6	1007	1777	1425	1582.2	1476								Y	33	28	N		
2	8.5												3201	4408	4237	3547	2992	1500												Y	40	96	N		
3													2212.5	2455	2070.6	1271.5	44.8													Y	39	60	N		
4	9.3	9.4	9.8										3030	3297	3297	3151	2195	2371	2212	3783	3622									Y	35	84	N		
5													3190	3009	2468	2245	2896													Y	39	60	N		
6	9.2	9.4	9.5	10.1	9.5								2451	2496.5	2482	2489	2073	2012	2007	1678	1559	1339								Y	34	48	N		
7	7.2	8											1317	1330	1288	1295													2	Y	36	132	N		
8	8.5												1996	1980	2004	2129														Y	22	48	N		
9													1185	1200	1206	1356														Y	16	21	N		
10													2069	1849	1707	628.7														Y	22	31	N		
11													2366	3119	3564	1015													2	Y	38	80	Y	19.5	20
12	8.27	8	8.4	8.6	8.7	8.9	8.8	9.3	9.6	10.2	9.7		160	871	988	2675	2513	1035			1232	1373	1383	1291	1923	2581	1883			Y	35	96	N		
13	8.8	8.4	8.7	8.6	8.1	8.9	9.4	10.2	10.4	10.1			5070	4197	3896	4230	2382	3503	2867	3436	4093	3343	3222	4482	4876				3	Y	36	96	Y	21	18
14	9.7	9.1	9.4	9.3	9.2	9.4	8.5	10.1					2451	3266	3827	2204	2007	2797	1910	2300	2323	2384	4569	3332					3	Y	36	48	N		
15		9.4	9.8	10	9.7	10.6	10.1	10.6					2480	2357	2348	2117			1976	1578	1329	1832	2238	1922					2	Y	25	24	N		
16													2933	4479	5696	8913													2	Y	40	84	N		
17	8.8	9.4	9.6	9.8	9.7	9.5	9.6						3139	2752	4671	3772	4500	2413	1500	3096	2529	2849	3511	3276					2	Y	37	11	N		
18	8.7												2366	2076	2211	2589														Y	33	72	N		
19													3133	3989	5225	5910													3	Y	40	132	N		
20													2130	2727	2478	1025														Y	40	6	N		
21													1650	2063	1954	861	1106													Y	28	24	N		
22	9.7	9.5	10										3324	3896	2865	2279														Y	25	33	Y	30	24
23	9.4	9.4											1779	1816	1796	1860	1301	893	686.7											Y	20	16	N		
24	8.7												2341	2664	2317	1052	1305	1419											3	Y	40	108	N		
25	10.1	9.8	9.4	9.9	9.8								2788	3926	3220	2561	2104	2101	1687	1575	2349	2565	3206						2	Y	43	14	N		
26													2356	3428	2986	2784	2436													Y	25	4	N		
27													2670	2043	1637	1860.3	1893.4												1	Y	34	96	N		
28													3200	1873	2167	2376	2452													Y	22	6	N		
29	8.6	8.9	8.8	9.1	10.2								1487	24919	1268	1199	1168	1174	766	1564	1479									Y	31	17	N		
30	10.2												1805	2199	2189	2036	1246	1160	942											Y	25	24	N		
31	9.4	9.2	8.9										3528	3378	3848	2571	3685	2131	2633	1716										Y	35	24	N		
32	9	9.2	9.1	9.2	8.7	9.7	10.1						2496	1706	1477	1604	1363	1377	1480	2423	1929	1715	2362	2815						Y	36	36	N		
33	9.6	10.2	9.7	9.6	9.8	10.2							1191	912	1497	1331	1495	1424	1331	2293	2281	1345	1403							Y	35	27	N		
34													2111	1792	1035															Y	31	28	N		
35													3034	2403	326															Y	30	24	N		
36	9.1	9.1											1141	1543	1862	1083													3	Y	30	144	N		
37													3793	3302	3001	2895														Y	30	14	N		
38													1672	1493	1600	1046													1	Y	40	65	N		
39													1420	1687	1789															Y	27	24	N		
40	8.4	8.6	8.5	8.7	9.2	10.1							2558	2845	1525	1558	1010	1683	1495	2021	3095	2138	1433						3	Y	35	36	N		
41	9.8	9	8.8	9.2	8.3	9.2							5149	1262	1099	1051	1086	1074	984	732	1805	877	1540						2	Y	30	36	N		
42	9	8.5											6936	6609	6780	5558	6578	5456	3405	3598	4786	4492	4500	3806	2999				4	Y	37	156	N		
43													1819	1807	1786	1396														Y	31	72	N		
44	8.4	8.5	8.3	8.9	9.8	9.3	8.7	10.1					1196	1032	684	603	451	1229	884	1351	866	783	643	600	512				4	Y	40	36	N		
45													2475	2223	1863	1786														Y	28	72	N		
46	9.9												2618	2963	2298	1702	2224	2065												Y	27	60	N		
47													1598	1070	1253	1250														Y	32	78	N		
48													2784	2795	2418	1606	886													Y	40	36	N		
49													2954	2759	1760	478													3	Y	27	96	N		
50	8.8	8.9	9.5	8.6	8.3	9.3	9.8	9.7	9.8	9.2	10.6		1754	3022	3172	2039	2387	2737	2454	2447	2068	1672	1975	2270	1590	2180			4	Y	36	36	N		
51	8.4	8.8											1200	1100	1124															Y	29	48	N		
52													1833	1722	1706															Y	33	36	N		
53													2403	2328	2155	1355														Y	20	17	N		
54	8.9	8.6	8.7										3108	3889	2920	1722	2009	1967	1143	2407									3	Y	30	84	Y	24	22
55	9.6	9.4	9.2	9.5	9.2								1466	991	1195	843	1086	1162	1528	2000	2298	2237							2	Y	33	52	N		
56	8.8	8.4	8.6	9.1	8.7	8.5	8.8						2471	1761	1463	1368	1363	1377	1202	2090	1892	1244	1873	2902					3	Y	36	132	N		
57	8.7	9	9										963	1275	1800	919	940	910												Y	25	4	N		
58													2691	2043	1637															Y	34	108	N		
59	9.3	9.5	9.1	9.2	9.6								4153	3848	4317	3343	3035	3161	2653	2535	2693	2000							2	Y	37	84	Y	30	84
60	9.5	9.2	9.3	9.1									1211	960	1081	775	985	1308	1329	1338	1138								3	Y	20	24	N		
61													3301	2589	3123	1982	1325													Y	26	24	N		
62	9.9	9.4	9.7	8.8	9.5	9.4							1914	1400	710	895	1150	897	1049	871	1172	1642	2433						4	Y	32	31	N		
63	9.5	9.1	9.3	8.7	9.2	9.5	9.1						1318	2228	2750	2020	1954	2330	1164	1673	2677	1816	2416	2399					4	Y	31	84	N		
64													3945	3882	2353	2949													4	Y	35	156	N		
65		9.7	9.2	9.5	9.8								1453		1543		1864		1422	1578	1329	1702							1	Y	25	20	N		
66	6.3	7	7.2										925																	Y	23	84	N		
67													1360	1947	1638	1647	710													Y	26	48	N		
68													2436	2083	3808	1547													2	Y	31	108	N		
69	8.2	7.8	8	7.7									4242	3273	3201	2621	2264	2687	2787	5459	3480								2	Y	39	72	N		
70	9.4												1388	1261	1306	1569	1468	1124												Y	31	60	N		
71	9.7	9.1	9.3	9.4	9.7	9.2	9.1						2884	2194	1860	1919	1313	920	1017	673	645	1183	1146	1959					4	Y	36	48	N		
72	10	10.6											1008	1194	1100															Y	25	24	N		
73	8.9	8.7	9.2	9.4	9.3								963	1275	1800	919	940	910	1129	749	989	1010							3	Y	36	36	N		
74	9.2	8.6	9.3	9.2									5138	4712	5188	2849	2072	2018	1339	2909	2284								2	Y	30	48	N		

S.No	DEFERIPRONE (USED)	MEAN DOSE (mg/kg)	months of exposure	COMBINATIONS	DOSE REDUCTION (YES/NO)	DECREASED IRON OVERLOAD	INCREASED URINARY PROTEIN	CARDIAC MRI -T2*	Y1 (2022)	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10 (2012)	LIVER MRI LIC	Y1 (2022)	Y2	Y3	Y4	Y5	Y6	Y7	Y8
1	N			DEFERASIROX	Y	Y			44		39.8									12		9.76					
2	Y	41	96	DEFERASIROX + DEFERIPRONE	N				38		33				41					1.99		8				4.65	
3	N			DEFERASIROX	N																						
4	Y	86	84	DEFERASIROX + DEFERIPRONE	N																						
5	Y	90	60	DEFERASIROX + DEFERIPRONE	Y	Y																					
6	Y	96	48	DEFERASIROX + DEFERIPRONE	Y	Y			43											1.1							
7	N			DEFERASIROX	N				37											6.8							
8	Y	90	22	DEFERASIROX + DEFERIPRONE	Y	Y																					
9	Y	88	35	DEFERASIROX + DEFERIPRONE	Y	Y																					
10	Y	78	42	DEFERASIROX + DEFERIPRONE	N																						
11	N			DEFERASIROX +DEFEROXAMINE	N				36		28									11		8.99					
12	Y	86	96	DEFERASIROX + DEFERIPRONE	Y	Y			42.2		31.8									4.2	6.8						
13	Y	80	96	DEFERASIROX + DEFERIPRONE + DEFEROXAMINE	Y	Y				12	18			14							14	12				9.67	
14	N			DEFERASIROX	Y		Y		31		30		29.8		34.7											26.9	
15	N			DEFERASIROX	Y	Y				22			35.1								4			3.7			
16	Y	83	84	DEFERASIROX+ DEFERIPRONE	Y	Y			21											4.2							
17	Y	90	11	DEFERASIROX + DEFERIPRONE	N					22	18.5		19								1.7	2		2			
18	Y	93	72	DEFERASIROX + DEFERIPRONE	N				24				12							1.6				3.8			
19	Y	80	132	DEFERASIROX + DEFERIPRONE	N						27			30								10			7.2		
20	Y	50	6	DEFERASIROX + DEFERIPRONE	Y	Y	Y																				
21	Y	87	24	DEFERASIROX + DEFERIPRONE	Y	Y																					
22	Y	20	33	DEFERASIROX + DEFERIPRONE+DEFEROXAMINE	Y																						
23	N			DEFERASIROX	N																						
24	Y	78	108	DEFERASIROX + DEFERIPRONE	Y						30		41		18							2.4		3.87		2.6	
25	Y	90	14	DEFERASIROX + DEFERIPRONE	Y	Y			33	22			42							6.83	7.83			1.8			
26	Y	66	4	DEFERASIROX + DEFERIPRONE	Y	Y			33		31.7									4.68		5.34					
27	Y	90	96	DEFERASIROX + DEFERIPRONE	Y		Y		27	30	31.7									1.88	2	2.5					
28	N			DEFERASIROX	Y	Y																					
29	N			DEFERASIROX	Y	Y			24.7											3.7							
30	N			DEFERASIROX	Y	Y																					
31	Y	75	24	DEFERASIROX + DEFERIPRONE	N																						
32	N			DEFERASIROX	Y	Y																					
33	Y	52	27	DEFERASIROX + DEFERIPRONE	Y																						
34	N			DEFERASIROX	Y	Y																					
35	Y	72	24	DEFERASIROX + DEFERIPRONE	Y	Y																					
36	N			DEFERASIROX	Y	Y			19.6		26									2.45		4.52					
37	Y	76	14	DEFERASIROX + DEFERIPRONE	Y	Y	Y																				
38	N			DEFERASIROX	N				16				14							13				16			
39	N			DEFERASIROX	N																						
40	Y	71	36	DEFERASIROX + DEFERIPRONE	Y		Y		32	33	27			28						0.7	0.9	1.2			1.4		
41	Y	93	36	DEFERASIROX + DEFERIPRONE	Y	Y			17		12									9.46		8					
42	Y	92	156	DEFERASIROX + DEFERIPRONE	N				13		14		19							8		11		9			
43	N			DEFERASIROX	N																						
44	Y	90	36	DEFERASIROX + DEFERIPRONE	N				24		34	27		34	40					10		7.23	9.6		4.98	15	
45	N			DEFERASIROX	Y	Y																					
46	Y	77	60	DEFERASIROX + DEFERIPRONE	Y																						
47	N			DEFERASIROX	Y	Y																					
48	N			DEFERASIROX	Y	Y																					
49	N			DEFERASIROX	Y	Y				25.4											3						
50	Y	75	36	DEFERASIROX + DEFERIPRONE	Y						36.4						38.9					7.9					
51	N			DEFERASIROX	N																						
52	N			DEFERASIROX	Y	Y																					
53	N			DEFERASIROX+ DEFEROXAMINE	Y	Y																					
54	N			DEFERASIROX+ DEFEROXAMINE	Y	Y			18	23		19								8.4	11	12	8				
55	N			DEFERASIROX	Y				42											15.8							
56	N			DEFERASIROX	Y	Y			23	34	35									4.76	8.5	6.8					
57	N			DEFERASIROX	N																						
58	N			DEFERASIROX+ DEFEROXAMINE	N																						
59	N			DEFERASIROX+ DEFEROXAMINE	N				14.7	18		15	11							5.7	5		7.4	8.3			
60	N			DEFERASIROX	Y				35.1		23	28			37	40				0.44		0.8	0.78			1	
61	Y	80	30	DEFERASIROX+ DEFERIPRONE	Y	Y																					
62	N			DEFERASIROX	Y	Y			18		23.56		39	33.2		29.5				0.78		0.8		1.4	1.1		0.99
63	N			DEFERASIROX+ DEFEROXAMINE	Y	Y				22	34	13		16		18					3.4	4.98	8.3		9			
64	N			DEFERASIROX+ DEFEROXAMINE	Y		Y				34					18						6.8					7
65	N			DEFERASIROX	Y		Y			33.4											5.32						
66	N			DEFERASIROX	N																						
67	N			DEFERASIROX	Y																						
68	N			DEFERASIROX	Y				24	19	22									1.4	2.3	1.98					
69	N			DEFERASIROX+ DEFEROXAMINE	Y				16	18	13									7	5.6	11					
70	N			DEFERASIROX	Y												34.3										
71	N			DEFERASIROX	Y	Y			19		31	29		28						3.6		1.8	2.94		1.1		
72	N			DEFERASIROX	Y	Y																					
73	N			DEFERASIROX + DEFERIPRONE	Y				23	32	29									1.8	1.44	0.99					
74	Y	32	12	DEFERASIROX	N				19	13	16									13	14	17					

S.No	Y9	Y10 (2012)	ADVERSE EFFECT (CTCAEVER -5)	RASH	PAIN ABDOMEN	NAUSEA	VOMITING	NEUTROPENIA	THROMBOCYTOPENIA	RISE IN SERUM CREATININE	RAISED AST/ALT	VISUAL DEFECTS	AUDITORY DEFECTS	OUTCOME (RESUMED/ STOPPED)
1				0	2	1	0	0	0	0	0	N	N	R
2				0	0	0	1	0	2	0	0	N	N	R
3				0	1	2	0	0	0	0	0	N	N	R
4				0	2	0	0	1	0	0	0	N	N	R
5				0	0	0	0	0	0	2	0	Y	N	R
6				0	1	0	0	0	0	0	0	N	Y	R
7				0	0	0	0	0	2	0	1	Y	N	R
8				0	0	0	2	1	0	0	0	N	N	R
9				0	0	0	0	0	0	0	1	N	N	R
10				0	0	0	1	0	2	0	0	N	N	R
11				0	0	1	0	0	0	0	0	N	N	R
12				0	1	1	1	0	0	0	0	N	N	R
13				0	0	1	0	0	0	0	2	N	N	R
14	6.8			0	1	0	0	0	2	0	1	N	N	S
15				1	0	0	0	0	0	0	0	N	N	R
16				0	0	0	1	0	0	2	0	Y	N	R
17				0	0	1	0	2	0	0	0	N	N	R
18				0	0	0	1	0	0	0	0	N	N	R
19				0	0	0	2	0	0	0	0	N	N	R
20				2	0	0	0	0	0	0	1	N	N	S
21				0	0	2	0	1	0	0	0	Y	N	R
22				0	0	0	0	0	2	2	3	N	N	S
23				0	0	0	1	0	0	0	2	N	Y	R
24				0	0	0	0	1	0	0	0	N	N	R
25				0	1	0	0	0	0	0	0	N	N	R
26				0	0	0	0	1	2	0	0	N	N	R
27				0	0	2	1	0	0	0	0	N	N	R
28				0	2	1	0	0	0	0	0	Y	N	R
29				2	0	0	0	0	0	0	1	N	N	R
30				0	1	0	2	0	0	0	0	N	N	R
31				0	0	0	1	0	0	0	0	N	N	R
32				1	0	0	0	0	0	0	2	N	Y	R
33				0	0	0	1	0	0	0	0	N	N	R
34				0	0	0	0	2	0	0	1	N	N	R
35				0	2	0	0	0	0	0	0	N	N	R
36				2	0	0	0	1	0	0	0	N	N	R
37				0	2	0	0	0	0	0	0	N	N	R
38				0	0	0	0	0	2	0	0	N	N	R
39				0	0	0	0	0	0	0	2	N	N	R
40				0	0	0	0	0	0	0	0	N	N	R
41				0	0	0	0	1	0	0	0	N	N	R
42				0	0	0	1	0	2	0	0	N	N	R
43				0	1	2	0	0	0	0	0	N	N	R
44				0	2	1	0	0	0	0	0	N	N	R
45				2	0	0	0	1	0	0	0	N	N	R
46				0	0	2	0	0	0	0	0	N	N	R
47				0	0	0	0	1	0	2	0	N	N	R
48				0	0	0	0	0	0	0	1	N	N	R
49				0	0	0	0	0	0	2	0	N	N	R
50	8.45			0	0	1	2	0	0	0	0	N	Y	R
51				2	0	0	1	0	0	0	0	N	N	R
52				0	0	0	0	1	0	0	0	N	N	R
53				0	0	1	0	0	0	0	0	Y	N	R
54				0	2	0	0	0	1	0	0	N	N	R
55				0	0	0	2	1	0	0	0	N	N	R
56				0	0	0	0	0	0	0	2	N	N	R
57				0	1	0	0	0	0	0	0	N	N	R
58				0	0	0	0	0	0	2	0	N	N	R
59				0	0	2	0	0	0	0	0	N	Y	S
60				2	1	0	0	0	0	0	0	N	N	R
61				0	0	0	0	0	2	0	0	Y	N	R
62				2	0	0	0	0	0	0	0	N	Y	R
63				0	0	1	0	0	0	0	0	N	Y	R
64				0	2	0	0	0	0	0	0	N	N	R
65				0	0	0	0	1	0	0	0	N	N	R
66				0	1	0	0	0	0	0	0	N	N	R
67				0	0	0	0	0	1	0	0	N	N	R
68				0	1	0	0	0	0	2	0	N	N	R
69				2	0	0	0	0	0	0	1	N	N	R
70	5.5			0	0	0	0	1	0	0	0	N	N	R
71				0	0	0	0	0	0	0	1	N	N	R
72				0	2	0	0	1	0	0	0	N	N	R
73				0	1	0	0	0	2	0	0	N	N	R
74				0	0	0	0	0	1	0	0	N	N	R

S.No	Name	DOB	AGE AT ASSESSMENT (MONTHS)	AGE (YEARS)	Sex	Locality	A+	A-	B+	B-	AB+	AB-	O+	O-	weight (actual)	weight (expected)	Weight (interpretation)	Height (actual) CM	Height (expected)	Height (interpretation)	BMI (actual)	BMI (Expected)	BMI (interpretation)	Anti Hbs	anti HCV	HCV- RNA	HIV	HbsAg	Hb F (FATHER)
75	M	24/11/2005	204	17.0	F	U	Y								48	52	2	149	153	1	21.6	22	2	positive	negative	negative	negative	negative	
76	AD	25/12/2011	132	11.0	M	R			Y						27	25	0	138	136	1	14.2	14	0	positive	negative	negative	negative	negative	0.5
77	MS	16/03/2016	88	7.3	M	R					Y				23	26	2	124	128	2	15	15.3	1	positive	negative	negative	negative	negative	
78	HS	11-07-2020	34	2.8	M	R			Y						11	14	2	93	97	3	12.7	13	0	positive	negative	negative	negative	negative	1
79	V	17/9/2018	54	4.5	M	U							Y		14	17	2	102	105	2	13.5	13.8	0	positive	negative	negative	negative	negative	0.4
80	R	02-11-2009	168	14.0	F	U			Y						38	40	0	141	143	0	19.1	19.3	2	positive	negative	negative	negative	negative	
81	R	09-04-2016	72	6.0	F	U			Y						21	24	2	121	125	2	14.3	14.6	0	positive	negative	negative	negative	negative	0.7
82	T	13/6/2017	66	5.5	F	U			Y						16	18	2	108	110	2	14	14.2	0	positive	negative	negative	negative	negative	0.8
83	JK	24/4/2018	6	0.5	F	U			Y						17	19	2	110	113	3	14	14.2	0	positive	negative	negative	negative	negative	0.5
84	IK	03-07-2006	204	17.0	F	U			Y						56	60	3	154	158	2	23.6	24	2	positive	negative	negative	negative	negative	
85	K	01-07-2012	132	11.0	F	U			Y						32	35	2	138	141	2	16.8	17	2	positive	negative	negative	negative	negative	
86	MK	19/5/2006	198	16.5	F	U							Y		56	59	3	153	155	1	23.9	24	2	positive	negative	negative	negative	negative	
87	A	31/12/08	168	14.0	M	U	Y								38	41	1	153	155	2	16.2	16.5	2	positive	negative	negative	negative	negative	1
88	JS	01-12-2010	162	13.5	M	U					Y				54	58	3	152	155	2	23.4	23.8	2	positive	negative	negative	negative	negative	1
89	R	07-08-2008	180	15.0	M	U			Y						36	40	0	155	158	1	16.6	17	0	positive	negative	negative	negative	negative	4.5
90	RS	08-08-2017	60	5.0	M	U		Y							15	14	1	107	105	1	13.1	13	0	positive	negative	negative	negative	negative	1.4
91	JK	28/09/07	192	16.0	F	R			Y						38	42	1	148	151	1	17.3	17.6	0	positive	positive	positive	negative	negative	
92	A	18/7/11	138	11.5	F	U					Y				21	24	0	128	131	0	12.8	13	0	positive	negative	negative	negative	negative	0.9
93	S	16/11/18	60	5.0	M	U				Y					18	20	2	110	112	3	14.9	20	0	positive	negative	negative	negative	negative	2
94	R	20/11/19	36	3.0	M	R							Y		11	14	1	91	93	0	13.3	13.5	0	positive	negative	negative	negative	negative	
95	MS	29/12/18	57	4.8	M	U			Y						14	12	2	93	90	2	16.2	16	2	positive	negative	negative	negative	negative	
96	R	01-01-2015	96	8.0	F	R							Y		20	24	1	90	95	2	24.7	25	2	positive	negative	negative	negative	negative	12.9
97	R	20/11/19	38	3.2	M	R							Y		11	13	0	91	94	1	13.3	13.5	0	positive	negative	negative	negative	negative	
98	S	31/1/08	180	15.0	M	U	Y								26	29	0	135	138	0	14.3	14.6	0	positive	positive	negative	negative	negative	
99	GS	16/10/13	108	9.0	M	R	Y								24	28	1	133	137	2	13.6	14	0	positive	negative	negative	negative	negative	
100	P	10-09-2010	144	12.0	M	R							Y		38	36	1	153	150	2	16.2	16	1	positive	negative	negative	negative	negative	
101	P	21-07-2007	156	13.0	F	U					Y				37	35	0	147	145	0	17.1	17	1	positive	negative	negative	negative	negative	0
102	HK	27/7/18	57	4.8	F	R					Y				13	16	1	106	109	2	11.6	12	0	positive	negative	negative	negative	negative	1
103	T	06-06-2017	68	5.7	F	R			Y						17	20	2	110	112	1	14	14.2	0	positive	negative	negative	negative	negative	
104	S	26/12/14	96	8.0	M	U							Y		29	32	2	126	130	3	18.3	18.7	2	positive	negative	negative	negative	negative	1
105	G	26/10/13	120	10.0	M	U	Y								32	35	3	134	137	2	17.8	18	2	positive	negative	negative	negative	negative	
106	K	28/07/16	84	7.0	M	R			Y						22	20	2	125	123	1	14.1	14	0	positive	negative	negative	negative	negative	0.6
107	A	24/4/14	108	9.0	M	R			Y						38	41	3	129	131	2	22.8	23	2	positive	negative	negative	negative	negative	0.8
108	K	09-06-2015	72	6.0	M	U			Y						18	21	2	120	124	2	12.5	12.7	0	positive	negative	negative	negative	negative	0.8
109	N	01-12-2008	180	15.0	M	U	Y								40	37	0	147	144	0	18.5	18.2	1	positive	negative	negative	negative	negative	0.3
110	MS	14/11/16	72	6.0	M	U			Y						18	21	2	120	124	2	12.5	12.7	0	positive	negative	negative	negative	negative	0.8
111	B	16/01/18	60	5.0	M	U							Y		17	20	2	107	110	3	14.8	15	1	positive	negative	negative	negative	negative	0.1
112	H	04-04-2009	168	14.0	M	U	Y								51	53	2	155	158	1	21.8	22	2	positive	negative	negative	negative	negative	6.4
113	J	24/5/16	84	7.0	M	R							Y		23	26	3	125	128	3	14.7	15	0	positive	negative	negative	negative	negative	6.9
114	H	16/7/07	186	15.5	M	U							Y		40	44	1	158	161	2	16	16.2	0	positive	negative	negative	negative	negative	
115	A	31/10/06	204	17.0	M	U							Y		31	30	0	148	146	0	14.2	14	0	positive	negative	negative	positive	negative	3.4
116	N	07-04-2010	132	11.0	M	U			Y						38	40	2	144	147	1	18.3	18.5	2	positive	negative	negative	negative	negative	1.3
117	RN	09-12-2007	192	16.0	M	U							Y		50	48	2	176	174	3	16.1	16	0	positive	negative	negative	negative	negative	
118	K	02-10-2019	48	4.0	F	U			Y						14	16	2	104	106	2	12.9	13	0	positive	positive	negative	negative	negative	0.3
119	PK	25/8/09	168	14.0	F	R			Y						30	33	0	151	154	1	13.2	13.4	0	positive	negative	negative	negative	negative	
120	MA	07-06-2020	38	3.2	M	U				Y					12	14	0	93	95	2	13.9	14	0	positive	negative	negative	negative	negative	
121	PS	18/11/07	186	15.5	M	U							Y		39	41	0	153	155	0	16.9	17	2	positive	negative	negative	negative	negative	
122	N	24/10/17	63	5.3	F	U				Y					20	22	3	114	116	2	15.4	15.5	2	positive	negative	negative	negative	negative	5.6
123	S	10-06-2014	96	8.0	M	U							Y		34	37	3	131	134	2	19.8	20	2	positive	negative	negative	negative	negative	1.3
124	R	05-11-2013	120	10.0	F	R			Y						22	25	0	126	128	0	13.9	14	0	positive	negative	negative	negative	negative	
125	V	17/2/13	120	10.0	M	U	Y								26	28	1	142	144	3	12.9	13	0	positive	negative	negative	negative	negative	0.5
126	R	06-05-2011	138	11.5	M	U			Y						28	27	1	146	144	2	13.1	13	0	positive	negative	negative	negative	negative	
127	R	03-02-2015	48	9.0	F	U			Y						12	15	0	97	100	0	12.8	13	0	positive	negative	negative	negative	negative	0.4
128	R	18/8/18	54	4.5	M	U			Y						15	18	2	109	112	2	12.6	13	0	positive	negative	negative	negative	negative	0.8
129	r2	30/7/17	60	5.0	F	U			Y						17	20	2	110	112	2	14	14.2	0	positive	positive	negative	negative	negative	1.2
130	K	31/12/08	168	14.0	M	U	Y								38	35	1	153	150	2	16.2	16	0	positive	negative	negative	negative	negative	1
131	A	22/03/21	28	2.3	M	U			Y						13	15	0	80	83	2	20.3	20.5	2	positive	negative	negative	negative	negative	
132	A	17/5/12	132	11.0	M	U			Y						30	28	0	125	122	2	19.2	19	2	positive	negative	negative	negative	negative	
133	PS	17/9/18	48	4.0	M	U	Y								13	15	1	96	99	1	14.1	14.3	0	positive	negative	negative	negative	negative	1.5
134	S	07-07-2016	80	6.7	F	R							Y		15	17	0	100	103	0	15	15.2	1	positive	negative	negative	negative	negative	0.9
135	D	26/12/17	60	5.0	F	U					Y				15	17	1	101	104	0	15	15.2	2	positive	negative	negative	negative	negative	
136	GS	31/7/16	78	6.5	M	R			Y						26	25	3	127	125	3	16.1	16	2	positive	negative	negative	negative	negative	7
137	HS	21/4/05	204	17.0	M	R							Y		60	62	3	162	164	2	22.9	23	2	positive	negative	negative	negative	negative	1.3
138	A	25/12/11	132	11.0	M	R			Y						27	30	0	138	140	1	14.2	14.4	0	positive	negative	negative	negative	negative	0.5
139	D	11-03-2008	174	14.5	M	U	Y								24	26	2	163	165	3	9	9.2	0	positive	negative	negative	negative	negative	0
140	IS	23/10/23	162	13.5	M	U			Y						28	30	3	153	155	3	12	12.1	0	positive	negative	negative	negative	negative	0.9
141	AA	02-09-2020	44	3.7	M	U							Y		12	14	0	93	95	0	13.9	14	0	positive	negative	negative	negative	negative	1.6
142	S	25/5/07	192	16.0	M	U									20	23	2	110	114	1	16.5	16.8	0	positive	negative	negative	negative	negative	0.4
143	S	23/3/09	168	14.0	F	R							Y		48	51	2	175	178	3	15.7	16	0	positive	negative	negative	negative	negative	91.7
144	S	08-03-2020	38	3.2	F	U							Y		10	13	0	83	85	0	14.5	14.7	0	positive	negative	negative	negative	negative	0.9
145	NA	09-02-2014	104	8.7	F	U							Y		23	25	2	120	122	1	16	16.2	2	positive	negative	negative	negative	negative	
146	GS	16/2/15	96	8.0	M	U							Y		28	31	3	130	133	3	16.6	17	2	positive	negative	negative	negative	negative	
147	L	04-05-2011	144	12.0	M	U			Y						29	32	2	137	140	2	15.5	15.8	2	positive	negative	negative	negative	negative	
148	J	20/2/16	84	7.0	F	U			Y						22	25	1	120	123	1	15.3	15.6	1	positive	negative	negative	negative	negative	6.8

S.No	HbA1 (Father)	Hb F (mother)	HbA1 (Mother)	MODIFIED KUPPUSWAMY SCALE	SES	AGE AT ENROLLMENT IN MONTHS	AGE AT DIAGNOSIS	date of assessment	AGE AT START OF CHELATION	COMPLIANCE	SPLENECTOMY	MENINGOCOCCAL VACCINE	PNEUMOCOCCAL VACCINE	formula for iron overload	annual transfusion requirement (Y0)-2022	transfusion_Y1	transfusion_Y2	transfusion_Y3	transfusion_Y4
75				12	3	18	9	23/11/13	96	Y	N	N	N	0.34	192	245	157	172	172
76	5.3	0.8	5.9	10	4	9	6.7	29/5/14	30	N	N	N	N	0.39	224	248	204	247	278
77				20	2	81	7	12-03-2022	88	N	N	N	N	0.45	258	234	206	223	213
78	4.9	1.5	5.2	18	2	15	7.3	08-01-2022	20	Y	N	N	N	0.33	186				
79	5.5	0.3	5.1	12	3	11	8.2	09-12-2019	12	Y	N	N	N	0.48	275	239	232		
80				10	4	72	6.2	09-07-2015	72	Y	N	N	N	0.39	220	263	256	226	308
81	7.4	2.9	6.7	10	4	12	6.1	29/12/18	26	Y	N	N	N	0.41	235	282	138	242	193
82	4.7	1	4.9	20	2	8	8	14/8/19	25	Y	N	N	N	0.4	227	247	186	180	
83	5.2	1.1	6.2	16	2	5	7.4	20/6/2019	14	Y	N	N	N	0.4	230	240	181		
84				10	4	204	9.4	24/04/23	204	Y	N	N	N	0.33	189	180	185	199	201
85				10	4	24	6.7	07-10-2014	27	Y	N	N	N	0.45	258	235	188	190	149
86				20	2	6	8.6	22/11/11	60	Y	Y	Y	Y	0.33	187	206	152	211	192
87	3.4	1.5	5.7	10	4	28	6.7	15/05/12	42	Y	N	N	N	0.45	258	281	204	197	257
88	4.7	0.9	6.1	10	4	10	6	02-07-2013	36	Y	N	N	N	0.31	175	226	182	205	218
89		6.3		10	4	8	8.4	16/11/12	53	Y	N	N	N	0.4	227	236	176	254	262
90	8.1	1.1	4	10	4	60	5.7	20/10/22	60	Y	N	N	N	0.46	262	215	189	209	211
91				12	3	120	6	10-12-2018	138	Y	Y	Y	Y	0.48	273	325	310	285	356
92	7.8	0.8	5.6	10	4	12	7.8	30/3/23	138	Y	N	N	N	0.27	155	160	186	177	182
93	5.5	1.7	6.1	10	4	36	6	19/2/21	36	Y	N	N	N	0.47	268	280	198	200	241
94				16	4	15	8.2	01-12-2023	36	Y	N	N	N	0.41	233	221			
95				12	3	8	4	07-07-2020	22	Y	N	N	N	0.02	146	150	160	160	
96	19.1	0.8	32.2	18	2	38	4.8	12-04-2018	48	Y	N	N	N	0.41	234	248	200	198	240
97				13	3	12	5.2	18/6/21	19	Y	N	N	N	0.41	233	221			
98				16	2	132	3	28/9/19	132	Y	N	N	N	0.48	272	317	255		
99				12	3	96	4.8	28/9/21	96	Y	N	N	N	0.7	404	16			
100				10	4	8	6	12-06-2013	36	Y	N	N	N	0.47	265	292	191	245	261
101	7.1	0	6.4	18	2	84	6.8	19/3/16	84	Y	N	N	N	0.41	236	254	193	272	225
102	6.6	7.5	2	16	2	48	11	02-06-2023	48	Y	N	N	N	0.49	280	266	234	206	230
103				10	4	15	10	02-12-2020	36	N	N	N	N	0.39	224	199	61	168	
104	4.5	1	4.3	10	4	6	18	28/12/16	48	Y	N	N	N	0.43	246	263	208	235	342
105				22	2	36	2.9	29/8/16	44	Y	N	N	N	0.41	236	270	241	248	181
106	5.8	1.81	4.4	20	2	48	7	15/2/21	60	Y	N	N	N	0.45	255	237			
107	5	0.8	4.7	16	2	12	6.7	19/11/15	18	Y	N	N	N	0.39	225	267	224	201	295
108	4.4	0.4	4.3	12	3	9	8	23/04/18	18	Y	N	N	N	0.53	304	280	226	275	123
109	8.5	0.6	4.8	17	2	84	5	04-03-2019	132	Y	N	N	N	0.38	216	214	175	247	269
110	4.4	0.4	4.3	12	3	9	6	23/04/18	18	Y	N	N	N	0.53	304	280	226	275	123
111	9	7	3	14	3	33	6.8	05-03-2021	42	N	N	N	N	0.43	245	275	300		
112		6.3		10	4	10	6.3	01-09-2013	48	Y	N	N	N	0.36	205	217	176	240	264
113		0.3	3.3	15	3	13	6	25/5/19	36	Y	N	N	N	0.44	248	293	227	233	215
114				20	2	156	7.8	23/9/20	156	Y	N	N	N	0.42	237	230	230		
115	1.7	3.7	3.7	10	4	9	8.5	15/01/13	84	Y	N	N	N	0.47	269	323	197	250	266
116	6.4	1.6	5.1	18	2	89	8.2	20/9/18	98	Y	N	N	N	0.42	242	247	85	228	245
117				22	2	120	8.3	09-05-2017	124	Y	N	N	N	0.41	235	208	152	226	154
118	6.2	0.9	4.9	12	3	6	11	10-09-2020	20	Y	N	N	N	0.35	202	196	153		
119		6.4	5.5	20	2	18	4.9	25/8/09	36	Y	N	N	N	0.42	240	227	194	250	260
120				22	2	9	5.8	09-01-2021	14	Y	N	N	N	0.46	262				
121		0.6	5.6	10	4	14	6.8	03-07-2012	60	Y	N	N	N	0.4	230	202	208	229	226
122		2.9		12	3	60	16	24/4/23	63	N	N	N	N	0.2	115	167	145	176	155
123	5.1	1	4.8	16	2	8	12	26/5/16	12	Y	N	N	N	0.42	240	260	193	243	153
124				14	3	96	10	10-03-2022	98	Y	N	N	N	0.21	120				
125	6	0.9	5.3	18	2	14	6.9	14/12/14	22	Y	N	N	N	0.47	268	278	215	188	138
126				10	4	120	6.3	31/10/22	120	N	N	N	N	0.34	195				
127	3	0.3	2.7	10	4	10	6.8	18/01/22	36	Y	N	N	N	0.3	173	135	171		
128	6.4	0.8	6.6	12	3	24	7	09-05-2020	25	Y	N	N	N	0.47	267	260	148		
129	5	3.9	4.5	14	3	24	7.8	10-07-2020	36	Y	N	N	N	0.52	298	283	207	142	
130	3.4	1.5	5.7	10	2	28	7.3	05-08-2012	48	Y	N	N	N	0.45	258	281	204	197	257
131				12	3	3	5	26/8/22	17	Y	N	N	N	0.36	207				
132				12	3	120	5.4	17/5/12	10	Y	N	N	N	0.37	208				
133	6	1	6.2	20	2	6	4.8	17/9/18	14	Y	N	N	N	0.39	223	198	143	185	
134	5.6	1.1	6.1	16	2	72	6	05-11-2023	82	Y	N	N	N	0.37	210	200	198	175	188
135				18	2	47	5.8	02-11-2022	48	N	N	N	N	0.48	273	218			
136				14	3	5	7.4	26/7/17	12	Y	N	N	N	0.36	206	227	215	275	230
137	5.7	1		10	4	12	8.6	08-05-2012	84	Y	N	N	N	0.23	130	178	210	214	213
138	5.3	0.8	5.9	10	4	9	7	26/5/14	36	Y	N	N	N	0.39	224	204	247	272	272
139	6	0.8	15.3	10	4	15	7.3	12-07-2013	48	Y	N	N	N	0.48				274	225
140	7.3	1.1	7.2	10	4	11	6.9	10-03-2017	96	Y	N	N	N	0.38					217
141	5.5	1.2	4.6	16	2	11	18	15/11/21	21	Y	N	N	N	0.4	234	216			
142	6.1	0.3	5.8	14	3	26	24	21/9/09	28	Y	N	N	N	0.37					
143	8.3	92.5	7.5	18	2	60	13	10-05-2019	120	Y	N	N	N	0.22	125	118	117		
144	5.7	2.1	5.6	17	2	24	11	30/8/20	24	Y	N	N	N	0.31	180				
145				26	1	78	18	31/3/21	78	Y	N	N	N	0.43	245	238			
146				16	2	36	5	09-06-2018	36	Y	N	N	N	0.38	218	269	224	295	
147				12	3	24	5.7	13/6/22	36	Y	N	N	N	0.39	225	234	265	226	
148	81.3	6.6	79.8	14	3	132	6.2	19/03/19	144	Y	N	N	N	0.4	228	236	230	205	258

S.No	transfusion_Y5	transfusion_Y6	transfusion_Y7	transfusion_Y8	transfusion_Y9	transfusion_Y10	transfusion_Y11	transfusion_Y12	transfusion_Y13	transfusion_Y14	transfusion_Y15	transfusion_Y16	mean transfusion	Total transfusion	Iron over load	Hb group	Average Hb (Y0)	Y1	Y2	Y3	Y4
75	219	160	203	230	232	238	247						224.27	2467	2664.36	4	10.2	10.1	9.2	10.1	10.7
76	272	312	231	291	207								251.4	2514	2715.12	3	9.7	9.7	9.3	9.3	9.3
77													226.8	1134	1224.72	2	8.6	8	8.2	8.4	8
78													186	186	200.88	3	9.7	9.7	9.6	9.4	9.6
79													248.66	746	805.68	3	9.8	9.8	9.8		
80	313	298	297										272.62	2181	2355.48	3	9.1	9.5	9.2	8.9	8.8
81													218	1090	1177.2	3	9.4	9.9	9.7	9.4	8.6
82													210	840	907.2	4	10.1	10.4	10.2	10.2	
83													217	651	703.08	3	9.2	9.3	9.9		
84													190.8	954	1030.32	2	8.3	8.8	7.8	7	8
85	305	261	270	270									236.22	2126	2296.08	3	9.6	9.7	9.7	9.5	10.2
86	216	218	171	189	184	232	210						215.27	2368	2557.44	4	10.5	9.8	8.8	9.7	9.9
87	259	284	217	201	290	260							270.8	2708	2924.64	3	9.1	9.3	8.5	8.7	8.6
88	139	239	298	194	211								208.7	2087	2253.96	3	9.7	9.2	9.6	9.4	8.5
89	298	267	280	288	259								254.7	2547	2750.76	3	9.4	9.8	9.3	9.3	9.1
90	247												222.16	1333	1439.64	3	9.3	9.5	9.9	9	9.79
91	415												327.33	1964	2121.12	2	7.9	7.7	7.9	7.8	7.8
92	158												169.66	1018	1099.44	3	9.6	9	9.9	9.5	9.9
93													237.4	1187	1281.96	2	8.7	8.7			
94													227	454	490.32	4	10.2	11.1			
95													154	616	665.28	3	9.4	9.2	9.4	9.6	
96													224	1120	1209.6	4	11.12	10.9	11	11.5	11.4
97													227	454	490.32	4	11.08	11.1	11.5	12	10.3
98													281.33	844	911.52	3	9.4	9.4	8.8		
99													210	420	453.6	2	8.5	8.9	8.6	8.8	8.5
100	246	277	305	240	228	178							272.8	2728	2946.24	4	10.3	9.5	9.5	9.1	9.1
101	246	230											236.57	1656	1788.48	3	9.5	9	9.3	8.5	8.7
102													243.2	1216	1313.28	2	7.9	7.6	8	8	7.8
103													163	652	704.16	2	8.8	9.5	8.3	9.3	
104	201	285	105										235.62	1885	2035.8	4	10	10.1	10.1	9.8	9.2
105	259	228											237.57	1663	1796.04	3	9.9	9.1	8.5	9.5	9.7
106													246	492	531.36	4	9.2	9	9.4	9.2	9
107	284	230	222										243.5	1948	2103.84	2	8.6	8.7	8.5	8.7	8.9
108													241.6	1208	1304.64	3	9.3	10.1	9.6	9.5	10.5
109	295	294	239										243.62	1949	2104.92	2	8.9	9.4	8.9	8.9	9
110													241.6	1208	1304.64	3	9.3	10.1	9.6	9.5	10.5
111													273.3	820	885.6	3	9.2	9.5	9.3	9.2	9
112	379	343	279	162	243								250.8	2508	2708.64	3	9.1	9.2	8.9	9.4	8.7
113	126												223.3	1342	1449.36	4	10	9.6	8.9	9.5	10.6
114													69.7	697	752.76	3	9.8	10	9.7		
115	250		266	247	239	225	218						211.53	2750	2970	3	9	8.5	9.1	9.4	9.5
116													174.5	1047	1130.76	2	8.5	8.7	8.8	8.4	8.8
117	108												180.5	1083	1169.64	2	8.7	8.9	9	8.7	9.4
118													183	551	595.08	3	9.4	9.3	9.5		
119	244	296	261	274	250	215	214						265.9	2925	3159	3	9.2	9.3	8.8	9.8	9.7
120													262	262	282.96	4	10.2	9.9	10	10.4	10.5
121	280	325	286	234	258								247.8	2478	2676.24	3	9.1	8.7	8.7	8.5	8.2
122													190	758	818.64	3	9.1	9.5	9.3	9.8	9
123	152	273											216.2	1514	1635.12	3	9.8	9.2	9.2	9.5	9.7
124													120	120	129.6	2	8.4	8	8.3	8.8	8
125	259	317	295										244.75	1958	2114.64	3	9.7	10.1	9.3	9.6	9.7
126													195	195	210.6	2	8.5	8.6	8	8.9	8
127													160	479	517.32	2	8.1	8.5	9.6	7	7.8
128													225	675	729	3	9	8.4	8.6		
129													232.5	930	1004.4	3	9.7	9.9	9.9	9.3	
130	259	284	276	290	260								256.6	2566	2771.28	3	9.3	9.3	8.5	8.7	8.6
131													207	207	223.56	3	9.7	10.2	9.2	9.4	9.3
132													208	208	224.64	2	8.2	8.9	8	8.6	8.4
133													187.25	749	808.92	4	10.3	11.5	10.5	11.1	
134													194.2	971	1048.68	3	9.1	9.5	9.3	9.9	9.1
135													245.5	491	530.28	3	9.8	9.8	9.8	9.8	
136	222												152.77	1375	1485	2	7.8	8.9	8.7	9.1	9.3
137	254	242	232	232									238.12	1905	2057.4	3	9.3	9.8	9.4	9.6	9.6
138	312	231	291	207									226	2260	2440.8	3	9.7	9.7	9.3	9.3	9.3
139	304	288	304	159	248								257.42	1802	1946.16	2	8.8			8.9	8.7
140	328	352	312	295	216								286.66	1720	1857.6	3	9.1				9.1
141													225	450	486	3	9.6	9.8	9.4	9.6	9.6
142							214	211					212.5	425	459	3	9.8				
143													120	360	388.8	3	9.8	9.7	9.5		
144													180	180	194.4	2	8	8	8.2	8	8
145													241.5	483	521.64	3	9.1	9.3	9.2	9	9.6
146													251.5	1006	1086.48	3	9.8	10.5	9.4	9.6	
147													237.5	950	1026	3	9.6	9.7	9.5	9.6	9.8
148													231.4	1157	1249.56	2	8.7	8.8	8.9	8.2	9.1

S.No	Y5	Y6	Y7	Y8	Y9	Y10	Y11	Y12	Y13	Y14	Y15	Y16	Serum Ferritin levels (SF0)	SF1	SF2	SF3	SF4	SF5	SF6	SF7	SF8	SF9	SF10	SF11	SF12	SF13	SF14	SF15	TANNERS STAGE (>10 years)	DEFERASIROX (USED)	MEAN DOSE (mg/kg)	months of exposure	DEFEROXAMINE (USED)	MEAN DOSE (mg/kg)	months of exposure
75	9.6	9.9	9.7	10.2	10.1	9.4	9.7						4414	4687	3890	2788	2712	3732	2498	2901	2881	2086	2568	3842					4	Y	38	96	Y	32	30
76	9.4	9.7	9.5	9.4	9.6								1060	1585	1510	2102	1870	1872	1715	1764	1385	819							1	Y	35	30	N		
77	8.7	9	9.4	8.8									1763	1456	1689	1632	1509	1539												Y	22	88	N		
78	9.3	9.6	9	9.2									1803	1800	1345	1673	1692	1890												Y	24	20	N		
79													2118	2081	2078															Y	28	12	N		
80	8.8	8.6	8.7										1331	888	1407	1426	1729	1827	2522	2160									3	Y	30	72	N		
81													1813	1851	1743	1083	829													Y	28	58	N		
82													2147	2902	2654	1711														Y	28	25	Y	32	25
83													2513	2460	2552															Y	40	14	N		
84	8.4	8.6	8.8	8	8.6	9	8.8	8.9					2130	2267	2003	1988													4	Y	18	204	N		
85	9.2	9.4	9.5	9.7									1207	1730	1745	1494	1486	1074	1321	1302	1625								1	Y	33	27	N		
86	8.8	8.7	9.4	9.7	10.1	10.2	9.7						2120	2846	2550	1580	1498	1270	1345	1480	1890	2050	1780	3160	2540				4	Y	37	60	N		
87	9	9.5	9.2	8.6	8.5	9							2212	2159	1687	1986	1125	1680	1350	2145	2545	2510	2440						3	Y	40	42	N		
88	9.3	9.7	9.5	9.3	9.2								2671	2345	2685	1775	1260	1475	2010	2255	2705	2614							2	Y	38	36	N		
89	9.7	9.5	9.3	9.8	9.4								2742	3435	2331	2941	2870	3313	2791	2405	2437								3	Y	34	53	N		
90	9	9.6	9.3	9	8.9								1456	1237	1368	1382														Y	30	60	N		
91	7.8												4486	3766	4042	3286	2070	2466											4	Y	41	138	Y	18.5	78
92	10	9.7											1358	1288	1342														1	Y	37	138	N		
93													2829	2725																Y	19	36	N		
94													2436	2263																Y	32	36	N		
95													2190	2598	1706															Y	38	20	Y	70	20
96	10.8												2046			2075	2305													Y	22	48	N		
97	10.5												2436	2263																Y	32	19	N		
98													3130	3989	5225														3	Y	41	132	N		
99	8												3896	5138																Y	37	96	Y	14	60
100	9.8	9	9.5	9.7	9.3	9.2							5149	4170	1071	1080	1086	1074	984	865	1565	816	1540						2	Y	31	36	N		
101	8.8	9.7											4914	5161	4854	3240	3868	4075	4867										3	Y	38	84	Y	96	84
102	7.8												3493	3345	3268	2345	2581	1936												Y	19	48	N		
103													5144	4000	3537	2010														Y	25	36	N		
104	9.7	9.5	9.8										3085	3083	3086	2511	2118	2951	2837	2693										Y	41	48	N		
105	9.6	9.4											5744	6519	4928	4108	3170	3212	3333											Y	39	44	N		
106	9.4												3190			1893	1888													Y	34	60	N		
107	9	9.1	9.2										3489	3814	3542	2635	4045	3387	2894	1637										Y	25	18	Y	26	18
108													2141	4085	2895	1907	1478													Y	35	18	N		
109	8.9	9.2	9.3										3128	3267	3087	2035	931	895	1564	1236									3	Y	34	132	N		
110													2141	4085	2895	1907	1478													Y	35	18	N		
111	9.5	8.9											2050	1874	1952	2105														Y	33	42	N		
112	9.2	9.1	8.8	8.9	9.2								2231	1732	2175	1837	1864	2265	2872	2833	2843	2819							3	Y	36	48	N		
113	9.5												1992	2522	2217	1510	1668	1182												Y	33	36	N		
114													3367	2838	3414														3	Y	37	156	N		
115	9	9.3	8.9	8.8	9.3	9.1							1318	2228	2750	2286	2442	2330	1164	1347	1878	1685	2416	1622					4	Y	37	84	N		
116													4034	5541	5924	3882	2992												2	Y	40	98	N		
117	8.6												1915	1674	1584	2263	2142	1811											4	Y	35	124	N		
118													3200	1873	2167															Y	22	20	N		
119	9.7	9.6	9.2	9.7	9.1	8.8	9.1						1627	1410	1993	2156	1744	1754	1538	1389	1697	1358	1765	1578					3	Y	40	36	N		
120	10	10.2	9.8										2325	2108	1935	1999	1853													Y	34	14	N		
121	8.4	8.6	8.3	8.2	8.5								2558	2845	1938	1347	1010	1683	1488	1909	3334	3095							3	Y	35	60	N		
122	9	9.1	8.7	8.9	9								2349	2200	2106	1933	1999	1823												Y	26	63	N		
123	9.2	9.3											1428	929	1007	1062	1080	1692	1585											Y	25	12	N		
124	8.9	8.2	9										905	996	1034	1100														Y	37	98	N		
125	9.9	9.5	9.4										4612	4339	3575	3796	3161	3531	1798	1584										Y	37	22	N		
126	8.3	8.8	8.6	9									1262	1238	1299	1327	1492													Y	38	120	N		
127	8												1783	1091	1335															Y	37	36	N		
128													4624	4132	2877															Y	26	25	N		
129													1990	2248	2164	1853														Y	28	36	N		
130	9	9.1	8.7	8.5	8.8								2108	2253	680	740	1215	1763	1774	2208	2535	2314							3	Y	35	48	N		
131	9.9	9.4	9.5										2459	2201	2286	2691														Y	28	17	N		
132	8	8.5	8.9	8.4	8.8	9	9.2						3156			4003	4999												1	Y	33	10	N		
133													2834	3254	2018	1019														Y	29	14	N		
134	9	9.4	8.3	8	9.9								2781	3149	3005	2893	2742	2399												Y	24	82	N		
135													649	1349	1291															Y	22	48	N		
136	9.8												1496	2382	1802	1619	1738	938												Y	34	12	N		
137	9.5	9.3	9.4	9.8									1938	2468	2375	2246	1890	2096	2192	1875	1969								4	Y	40	84	N		
138	9.4	9.7	9.6	9.2	9.1								950	1689	1694	1728	1930	1872	1715	2276	1384	1478							1	Y	36	36	N		
139	9.8	8.8	8.4	8.5	8.9								3120			2950	2533	2561	2328	2950	2640	2404							2	Y	39	48	N		
140	9	9.4	9.2	9.3	9.1								1488	1543		1231	1107	1431	1247	1581	1622	1140							2	Y	31	96	N		
141													1856	1578	1497	2300														Y	16	21	N		
142							9.4	9.9	10.1				2301		3428	2984	2278												3	Y	35	28	N		
143													1230	1093	1389														3	Y	36	120	N		
144													2000	2430	1988	1100	980													Y	27	24	N		
145	9	9											1590	1070	935															Y	27	78	N		
146													2993	3009	2616	1876														Y	35	36	N		
147	9.3	9.3	9.4	9.8									2614	2885	2200	1956													2	Y	36	144	N		
148													2239	3282	3103	1772	1586													Y	33	36	N		

S.No	DEFERIPRONE (USED)	MEAN DOSE (mg/kg)	months of exposure	COMBINATIONS	DOSE REDUCTION (YES/NO)	DECREASED IRON OVERLOAD	INCREASED URINARY PROTEIN	CARDIAC MRI -T2*	Y1 (2022)	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10 (2012)	LIVER MRI LIC	Y1 (2022)	Y2	Y3	Y4	Y5	Y6	Y7	Y8
75	N			DEFERASIROX+ DEFEROXAMINE+DEFERIPRONE	N				21	15	13		7.8		8.9					8	11	18		12		9.3	
76	N			DEFERASIROX	N				34											7.23							
77	N			DEFERASIROX	N												45.4										
78	N			DEFERASIROX	Y																						
79	N			DEFERASIROX+ DEFEROXAMINE	Y	Y																					
80	N			DEFERASIROX+ DEFEROXAMINE	Y				44	31		28								4.65	2.54		3.76				
81	N			DEFERASIROX	Y																						
82	N			DEFERASIROX+ DEFEROXAMINE	Y	Y																					
83	N			DEFERASIROX	Y	Y																					
84	Y	90	123	DEFERASIROX+ DEFERIPRONE	Y	Y				27.6		29									6.34		4				
85	N			DEFERASIROX	Y				45											2.2							
86	N			DEFERASIROX+ DEFEROXAMINE	Y				36.1	23	16	19			44.8					10	5	9			6.7		
87	N			DEFERASIROX	Y		Y		24		29	22								12.63		11.31	13				
88	N			DEFERASIROX+ DEFEROXAMINE	Y		Y			28		32					37.6				10		4.76					
89	N			DEFERASIROX	Y				29						36.1					8.6						12	
90	N			DEFERASIROX	Y	Y																					
91	N			DEFERASIROX+ DEFEROXAMINE	Y	Y			15		11	9.67		15						11		8.9	14		9.87		
92	Y	82	66	DEFERASIROX + DEFERIPRONE	Y	Y			28											4.85							
93	N			DEFERASIROX	Y																						
94	N			DEFERASIROX	N																						
95	N			DEFERASIROX+ DEFEROXAMINE	N																						
96	N			DEFERASIROX	N																						
97	N			DEFERASIROX	N																						
98	N			DEFERASIROX	N				17											11.99							
99	N			DEFERASIROX + DEFEROXAMINE	N					27					26.9		34.3				0.99							
100	Y	76	3	DEFERASIROX + DEFERIPRONE	N				44		28		39.4							7.56		8.98		6			
101	N			DEFERASIROX+ DEFEROXAMINE	Y		Y			29.44	39										2.5	1.99						
102	N			DEFERASIROX	Y	Y																					
103	N			DEFERASIROX+ DEFEROXAMINE	N																						
104	N			DEFERASIROX+ DEFEROXAMINE	N																						
105	N			DEFERASIROX	N				16											14							
106	N			DEFERASIROX+ DEFEROXAMINE	N																						
107	N			DEFERASIROX+ DEFEROXAMINE	N																						
108	N			DEFERASIROX	N																						
109	N			DEFERASIROX	N				22			32	26.5							1.1			2	1.85			
110	N			DEFERASIROX	N																						
111	N			DEFERASIROX	N																						
112	N			DEFERASIROX	N				22			28								4.2			12				
113	N			DEFERASIROX	N																						
114	N			DEFERASIROX	Y		Y				37.5				55.3		35.4					9.65				8.2	
115	N			DEFERASIROX	Y				22				15							18.4				14.6			
116	N			DEFERASIROX	Y	Y			16											15							
117	N			DEFERASIROX	Y	Y											32.9										
118	N			DEFERASIROX	Y	Y																					
119	N			DEFERASIROX	Y				18		22		15							3.6		2.56		2			
120	N			DEFERASIROX	Y		Y																				
121	N			DEFERASIROX	Y	Y			25	18	24		19							0.89	0.99	1.3		2			
122	N			DEFERASIROX	Y		Y																				
123	N			DEFERASIROX	Y																						
124	N			DEFERASIROX	Y	Y			25											1.55							
125	N			DEFERASIROX	Y	Y			28											9.97							
126	N			DEFERASIROX	Y				22		27									3.67		5.63					
127	Y	69	32	DEFERASIROX + DEFERIPRONE	Y																						
128	N			DEFERASIROX	Y																						
129	N			DEFERASIROX	Y																						
130	N			DEFERASIROX	Y				34	28	36									1.3	2	1.76					
131	N			DEFERASIROX	Y																						
132	N			DEFERASIROX	Y				20											5							
133	N			DEFERASIROX	Y	Y																					
134	N			DEFERASIROX	N																						
135	N			DEFERASIROX	N																						
136	N			DEFERASIROX	N																						
137	N			DEFERASIROX	N				24	19	29		33				32			13	12.54	13.5		14			
138	N			DEFERASIROX	N				18.8											6.99							
139	N			DEFERASIROX	N				24		28		18							4.78		7.3			6		
140	N			DEFERASIROX	N																						
141	N			DEFERASIROX	N																						
142	N			DEFERASIROX	N				22		20		19.45		16					14		14		11		2.6	
143	N			DEFERASIROX	N				21.2				33							15.21				10.43			
144	N			DEFERASIROX	N																						
145	N			DEFERASIROX	N																						
146	N			DEFERASIROX	N																						
147	Y	48	115	DEFERASIROX+ DEFERIPRONE	N				33	34										15	18						
148	N			DEFERASIROX	N																						

S.No	Y9	Y10 (2012)	ADVERSE EFFECT (CTCAEVER -5)	RASH	PAIN ABDOMEN	NAUSEA	VOMITING	NEUTROPENIA	THROMBOCYTOPENIA	RISE IN SERUM CREATININE	RAISED AST/ALT	VISUAL DEFECTS	AUDITORY DEFECTS	OUTCOME (RESUMED/ STOPPED)
75				0	0	0	0	1	0	0	0	N	N	R
76				0	0	0	0	1	0	2	0	N	N	R
77	3.3			0	1	0	2	0	0	0	0	N	N	R
78				0	2	0	0	0	0	1	0	N	N	R
79				2	0	0	0	0	0	0	1	N	N	R
80				0	0	2	0	0	0	1	0	N	N	R
81				0	0	1	0	0	0	0	0	N	N	R
82				0	2	0	0	0	0	0	0	N	N	R
83				0	0	0	0	2	0	0	0	N	N	R
84				0	0	0	0	1	0	0	0	N	Y	R
85				0	2	0	0	0	0	0	0	N	N	R
86				2	0	0	0	1	0	0	0	N	N	R
87				0	0	0	0	0	0	0	0	N	Y	R
88	9.2			0	0	0	0	0	0	0	0	N	N	R
89				0	0	0	0	0	0	0	0	N	N	R
90				2	0	1	0	0	0	0	0	N	N	R
91				0	0	0	0	0	0	2	1	N	N	R
92				2	0	1	0	0	0	0	0	N	N	R
93				0	0	0	0	0	2	0	1	N	N	R
94				0	0	0	2	0	0	0	0	Y	N	R
95				0	0	1	0	0	0	2	0	N	N	R
96				0	0	0	1	0	0	0	0	N	N	R
97				0	1	0	0	0	0	0	0	N	N	R
98				2	0	0	1	0	0	0	0	N	N	R
99	1.3			0	0	0	0	0	0	0	2	N	N	R
100				0	0	0	0	1	0	0	0	N	N	R
101				0	1	0	0	0	0	2	2	N	N	S
102				2	0	0	0	0	0	0	1	N	N	R
103				0	0	1	0	0	2	0	0	N	N	R
104				0	0	0	2	0	0	0	0	Y	N	R
105				1	0	0	0	0	0	0	0	N	N	R
106				0	0	2	0	0	0	0	1	N	N	R
107				1	0	0	0	0	0	0	0	N	N	R
108				0	2	0	0	1	0	0	0	N	N	R
109				0	1	0	0	0	0	0	2	N	N	R
110				0	2	0	0	1	0	0	0	N	N	R
111				0	0	0	0	0	0	2	0	N	N	R
112				0	0	0	0	1	0	0	0	Y	N	R
113				0	1	0	0	0	0	0	0	N	N	R
114	7.7			0	1	0	0	0	0	0	0	N	N	R
115				2	0	0	0	1	0	0	0	N	N	R
116				0	0	0	0	0	0	0	2	N	N	R
117	5.3			0	1	0	0	0	0	0	0	N	N	R
118				2	0	1	0	0	0	0	0	N	N	R
119				0	0	0	0	0	0	2	1	N	N	R
120				0	1	0	0	0	0	0	0	N	N	R
121				0	0	0	0	2	0	0	0	N	N	R
122				0	2	1	0	0	0	0	0	N	N	R
123				2	0	0	0	0	0	0	0	Y	N	R
124				0	0	0	0	1	0	0	2	N	N	R
125				0	0	0	1	0	0	0	0	N	N	R
126				0	2	0	0	3	0	0	0	N	N	R
127				0	0	0	1	0	0	0	2	N	N	R
128				2	0	0	0	0	0	0	0	N	Y	R
129				0	0	0	1	0	2	0	2	Y	N	R
130				0	2	0	0	0	0	0	0	N	N	R
131				0	0	0	0	1	0	0	0	N	N	R
132				0	2	0	0	1	0	0	0	Y	N	R
133				0	0	0	1	0	0	0	0	N	N	R
134				0	0	0	0	0	0	0	0	N	N	R
135				0	0	1	0	0	0	0	0	N	N	R
136				1	0	0	0	0	2	0	0	N	N	R
137	19			0	2	0	0	0	0	0	1	N	N	R
138				0	0	0	1	0	0	0	0	N	N	R
139				0	2	0	0	0	0	0	0	N	N	R
140				0	1	0	0	0	0	2	0	N	N	R
141				0	0	1	0	0	2	0	0	N	N	R
142				0	1	0	0	0	0	0	0	N	N	R
143				2	1	0	0	0	0	0	0	N	Y	R
144				0	0	1	0	0	0	0	0	N	N	R
145				0	0	0	0	1	0	0	0	N	N	R
146				2	0	0	0	0	0	0	0	N	N	R
147				0	0	0	1	0	0	0	2	N	N	R
148				0	2	0	0	0	0	0	1	N	N	R

Baba Farid University
of Health Sciences
Sadiq Road
Faridkot-151 203 (Pb). INDIA.
Phone : 01639-256232,256236
Tele/Fax : 01639-256235
Email – Thesisbfuhs@gmail.com

(45)

No. BFUHS/2K23p-TH/ 31 Date 1/1/24

The Principal
Dayanand Medical College & Hospital
Ludhiana

Subject:: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 25.09.2023 has approved the plan of thesis of **Veronica Banal**, a student of your college for **MD Paediatrics** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
An observational study of iron chelation practices in thalassemia day care centre of a tertiary care hospital in punjab .

Supervisor
Dr. Shruti Kakkar
Assoc. Prof.,
Dept. of Paediatrics

Co-Supervisor:-
Dr. Deepak Bhat
Professor
Dept. of Paediatrics

Co-Supervisor:-
Dr. Sandeep Kaushal
Prof. & Head
Dept. of Pharmacology

The student may submit the thesis in triplicate alongwith the plan in triplicate also, to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She may be directed to attach a photocopy of this letter with the forwarding letter while submitting thesis in the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic, if any.

Controller of Examinations

Note :

1. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*

AN OBSERVATIONAL STUDY OF IRON CHELATION PRACTICES IN THALASSEMIA DAY CARE CENTRE OF A TERTIARY CARE HOSPITAL IN PUNJAB

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

IN

PAEDIATRICS

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

AUGUST, 2022

DR. VERONICA BANAL

DEPARTMENT OF PAEDIATRICS
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	AN OBSERVATIONAL STUDY OF IRON CHELATION PRACTICES IN THALASSEMIA DAY CARE CENTRE OF A TERTIARY CARE HOSPITAL IN PUNJAB
For the degree of	MD PEDIATRICS
Name of the candidate	Dr. Veronica Banal
Supervisor	Dr. Shruti Kakkar Associate Professor, Department of Pediatrics, DMCH, Ludhiana
Co-Supervisor	Dr. Deepak Bhat, Professor, Department of Pediatrics, DMCH, Ludhiana Dr. Sandeep Kaushal, Professor& Head, Department of Pharmacology, DMCH, Ludhiana
Institution	Dayanand Medical College and Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: Thalassemia is a group of autosomal recessive disorders, leading to reduction in synthesis of globin chains required for hemoglobin synthesis. Worldwide 80-90 million people carry the beta thalassemia trait. In India 36 million people carry the responsible gene. Thalassemia major is the severe form of beta thalassemia characterized by fatigue, weakness, pallor, facial bone deformities, slow growth and splenomegaly. Blood transfusion (BT) remains the first –line treatment in these patients. Each unit of blood contains 200-250 mg elemental iron and causes iron overload, to prevent this, iron chelation therapy is recommended for these patients. Iron overload has been linked to prognosis with studies showing a near normal life if serum ferritin is maintained below 1000 although long term use of chelation may be associated with complications.

Aims and Objectives: To study the effect of various iron chelation practices in thalassemia day care centre of tertiary care hospital in Punjab.

Materials and Methods: A observational study that will be conducted on patients with transfusion dependent thalassemia registered in the Thalassemia day care centre in the Department of Paediatrics, Dayanand Medical College and Hospital, Ludhiana over a period of fifteen months.

Clinical significance: To compare the usage of different iron chelation therapies when used alone or in combination , their outcome, adverse effects and efficacy in patients of transfusion dependent thalassemia.

After this study, we will be able to study the outcome of various chelation regimen followed in various groups of patients.

Keywords: Chelation therapy, iron overload, thalassemia major, blood transfusion, deferasirox ,deferiprone, deferoxamine.

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"AN OBSERVATIONAL STUDY OF IRON CHELATION PRACTICES IN THALASSEMIA DAY CARE CENTRE OF A TERTIARY CARE HOSPITAL IN PUNJAB"** exist in the Department of Pediatrics at Dayanand Medical College and Hospital, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis are genuine and is collected by the candidate herself under our supervision and guidance.

Supervisor

Dr. Shruti Kakkar
Associate Professor
Department of Pediatrics
DMCH, Ludhiana

Co-Supervisor

Dr. Deepak Bhat
Professor
Department of Pediatrics
DMCH, Ludhiana

Dr. Sandeep Kaushal
Professor & Head
Department of Pharmacology
DMCH, Ludhiana

Head of the Department

Dr. Puneet Aulakh Pooni
Professor & Head
Department of Pediatrics
DMCH, Ludhiana

Place : _____

Date : _____

APPROVAL PROFORMA
BY
RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Veronica Banal
Department	Pediatrics
Topic of Thesis	AN OBSERVATIONAL STUDY OF IRON CHELATION PRACTICES IN THALASSEMIA DAY CARE CENTRE OF A TERTIARY CARE HOSPITAL IN PUNJAB
Likely date of appearing in PG examination	May/ June, 2024
Date of enrollment	7th March 2022
Name of Head of Department	Dr. Puneet Aulakh Pooni
1) Supervisor **2) Co-Supervisor**	Dr. Shruti Kakkar Dr. Deepak Bhat Dr. Sandeep Kaushal
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
Dr. Jaspal Singh (Professor & Head, Surgery)	Dr. Ramit Mahajan (Associate Professor, Gastroenterology)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)	Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)
Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal & Professor & Head, Cardiology)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / ~~No~~

Dr. Sandeep Puri
Chairperson
Research Committee

Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairperson
Ethics Committee

Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	Dr. VERONICA BANAL H. No. 6A ,NEW GOBIND NAGAR JALANDHAR CITY 144002
2	NAME OF THE INSTITUTE	Dayanand Medical College and Hospital, Ludhiana
3	COURSE OF STUDY AND SUBJECT	MD Paediatrics
4	DATE OF ADMISSION OF COURSE	7th March 2022
5	TITLE OF THE TOPIC	AN OBSERVATIONAL STUDY OF IRON CHELATION PRACTICES IN THALASSEMIA DAY CARE CENTRE OF A TERTIARY CARE HOSPITAL IN PUNJAB

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

The term “thalassemia” is made by joining two greek words “thalessa”(sea) and “haema”(blood) which refers to disorders associated with defective synthesis of α- or β-globin subunits of hemoglobin HbA(α2 β2),and inherted as pathological alleles of one or more of the globin genes which are located on chromosomes 11(β) and 16(α). The clinical manifestations are divers ranging from absence of symptoms to profound fatal anemias in utero,or,if untreated,in early childhood.

The thalassemia syndrome is classified according to the affected globin chains i.e either α or β. There are two major groups, α- and β-thalassemia,which are further subclassified according to absent (αo and βo) or reduced (α+ or β+) globin chain synthesis.The overall prevalence of β-thalassemia trait was 2.78 % and varied from 1.48 to 3.64 % in different states of India.[1]

β-Thalessemia syndromes

β-thalassemia major (also called Cooley anemia, Mediterranean anemia, and von Jaksch anemia) denotes the homozygous or compound heterozygous forms of the disease, which are characterized by severe anemia (range, 1-7 g/dL of Hb), hemolysis, and massive ineffective erythropoiesis.Clinical manifestations appear in infancy and include severe anemia characterized by extreme pallor, jaundice, or failure to thrive, accompanied by poor feeding, irritability, decreased activity, and/or increased somnolence.[2]Typical Thalessemic facies, features of which are

1.frontal bossing

2. maxillary hypertrophy

3.depression of nasal bridge

4. malocclusion of teeth.

Untreated, it is usually fatal in the first few years of life.[3]increased resorptive rates and suppression of osteoblast activity, resulting in diminished bone mineral density (BMD) more evident in the lumbar spine.

The diagnosis of β-thalassemia major is readily made during childhood on the basis of clinical features, profound microcytosis,tear drop cells, target cells a characteristic blood smear and elevated levels of HbF, HbA_2, or both. The only management of such patients is blood transfusion at regular intervals.Many patients require regular blood transfusion therapy to maintain a hematocrit of at least 27 to 30% so that the erythropoiesis is suppressed.However chronic blood transfusion therapy can lead to blood borne infections,alloimmunization,febrile reactions and lethal iron overload.[4]

Iron overload

Normally iron absorption and loss are balanced at about 1 mg/day. Transfused blood contains 200-250 mg of iron per unit. Hence, patients with β-thalassemia major (TM) receiving 3-5 units of blood per month have an annual intake of 5000-12,000 mg of iron or 0.3-0.6 mg/kg per day there is a rise in Hb of 0.5-1.2 mg/dl.[5]Patients with TM absorb excess iron despite iron overload because of production of GDF15 and possibly other proteins (eg, TWSGI) from erythroblasts,which inhibit hepcidin synthesis.[6]IT is not possible for the human body to excrete this excess iron.[7]Ferritin can possibly be used as screening and monitoring tool for iron load in TI patients when other modalities to assess iron overload are not easily available.

Untreated transfusional iron load results in damage to the liver,[8] endocrine organs, and most importantly to the heart. therefore, without effective iron chelation, death occurs from cardiac failure[9] usually in late childhood or in the teenage years.[10] Iron chelation therapy has proven to be the only option to reduce morbidities and prolong survival of these children.[11]The rapid accessibility of the oral chelatorsdeferasirox and deferiprone to intracellular labile iron compartments renders them potentially efficacious for protection from and possibly reversal of cardiac damage induced by iron overload.

Properties of an ideal chelator[12]

- Patient acceptance/compliance
  - Good Oral bioavailability

- Suitable for monotherapy
- Good body iron control
  - High chelating efficiency
  - High and specific affinity for Fe^{3+}
- Acceptable toxicity-efficacy profile
- Simplicity and ease of monitoring
- Minimal toxicity

Goals of chelation therapy

The goal of chelation is to maintain “safe” iron levels among the patients having iron load from transfusion therapy. Ideally, chelation should be administered in a way to prevent excess iron accumulation and the resulting hepatic, endocrinologic, and cardiac complications by matching the ongoing transfusional iron intake.[13]Chelators also bind non transferrin-bound and labile plasma iron, protecting vulnerable organs such as the heart from damage by these toxic iron forms, and continuous chelator exposure is optimal in this regard.

Three iron chelators have been in use:

- Deferoxamine
- Deferiprone
- Deferasirox

Deferoxamine (DFO; Desferal and generic)

Deferoxamin is a hexadentate chelator, thatbinds iron tightly e has been the standardiron chelator since the 1970s. This drug is both safe and effectivefor transfusionalhemosiderosis., and the iron-DFO complex is excreted inboth urine and stool. DFO is administered as long parenteralinfusions because the plasma half-life is short (10-30 minutes) andit is not active orally.[14]Thus, it is given as an overnight subcutaneousinfusion 5 to 7 nights/wk.

Deferiprone

Deferiprone is an oral drug which is active hydroxypyridin.It was first used in humans in 1987. Deferiprone is a bidentate chelator(3 molecules surround one iron ion.)half of life of deferiprone is 1.9 hours.

The iron(III) chelate of deferiprone carries no netcharge and therefore can penetrate membranes easily,that allows the removal of potentially toxic iron from tissues. Controversy over the safety of deferipronearose in the late 1990s because of an observation of hepaticfibrosis during a clinical trial.[15]Deferiprone oftencauses gastrointestinal symptoms.Deferiprone showed less myocardial iron burden and better global systolic ventricular function The side effects that are potentially severe include erosive arthritis andneutropenia (up to 5% of patients), including severe agranulocytosis(up to 0.5% of patients);therefore close monitoring is required. Typical dosage for deferiprone is 75 mg/kg/d in 3 divided doses, upto 100 mg/kg daily.

- **Deferasirox**

  Deferasirox (ICL670, Exjade) belongs to a new class of oraltridentate chelators, N-substituted bis-hydroxyphenyltriazoles.[16]Deferasirox, has a plasma half-life of 8 to 16 hours, once-daily dosing permits the circulating drug to scavenge non–transferrin-bound"labile plasma iron," the chemical species responsible fortissue damage in iron-overloaded subjects',[17] by means of toxicoxygen intermediaries. Deferasirox-iron complexes are excretedin the stool.

  In our hospital we use this combination therapy for chelation in chronically transfused thalessemic children in doses of 10 mg/kg of deferasirox-single dose and hiked upto 30-40mg/kg as per the requirement of the patient.[18]DFX has always been used as a single daily dose drug.

  Thus this study has been planned for comparing the efficacy and safety of deferasirox and other 2 drugs when given in single vs divided doses for chelation therapy in patients with thalassemia.

6.2 REVIEW OF LITERATURE

Iron chelation therapy is an inevitable treatment for the iron overload and preventing it harmful effects in human body. Multiple studies have been conducted across the world, for comaparing the effectiveness, tolerability and safety of various iron chelators as a monotherapy or in combination.

1. Hoffbrand et al(2012) conducted a study How I treat transfusional iron overload which mainly focused on the use of MRI to determine which adult and pediatric patients need to begin iron chelation therapy to determine which adult and pediatric patients need to begin iron chelation therapy and to monitor their progress.[1]
2. Cappellini et al(2011) conducted a study on iron chelation with deferasirox in adult and pediatric patients with thalassemia major: efficacy and safety during 5 years' follow-up. To evaluate long-term efficacy and safety of once-daily oral iron chelation with deferasirox, patients aged >2 years who completed a 1-year, phase 3, randomized trial entered a 4-year extension study, either continuing on deferasirox (deferasirox cohort) or switching from deferoxamine to deferasirox (crossover cohort). **.** This first prospective study of long-term deferasirox use in pediatric and adult patients with thalassemia suggests treatment for <5 years is generally well tolerated and effectively reduces iron burden.[2]
3. Cappellini et al(2006) conducted a study on iron chelation with deferasirox in adult and pediatric patients with thalassemia major: efficacy and safety during 5 years' follow-up conducted a study to evaluate long-term efficacy and safetyof once-daily oral iron chelation with deferasirox,patients aged >2 years.This first prospective study of long-term deferasirox use in pediatric and adult patients with thalassemia suggested treatment for <5 years is generally well tolerated and effectively reduces iron burden.[4]

4. Cohen et al(2008) conducted a study on effect of transfusional iron intake on response to chelation therapy in thalassemia major.It revealed Splenectomized patients had lower transfusional iron intake and greater reductions in iron stores than patients with intact spleens.Transfusional iron intake should be monitored on an ongoing basis in thalassemia major patients, and the rate of transfusionaliron loading should be considered when choosing the appropriate dose of an iron chelating agent.[3]

5. Berdoukas et al (2010)conducted a study on in search of the optimal iron chelation therapy for patients with thalassemiamajor iron cardiomyopathy is the most common cause of death in patients with transfusion dependent anemia. Improvement has been attributed in part to greater iron chelation options and the ability to recognize pre-clinical cardiac iron deposition by Magnetic Resonance Imaging studies (MRI). Patients with low cardiac T2*, as measured by MRI, have a significant risk of period if changes to their chelation regime are not made.[8]

6. Pepe et al(2011)conducted study on deferasirox, deferiprone and desferrioxamine treatment in thalassemia major patients: cardiac iron and function comparison determined by quantitative magnetic resonance imaging .Myocardial iron concentrations were measured by T2* multislicemultiecho technique. Biventricular function parameters were quantitatively evaluated by cine images. Liver iron concentrations were measured by T2* multiecho technique. The global heart T2* value was significantly higher in the deferiprone (34±11ms) than in the deferasirox (21±12 ms) and the desferrioxamine groups (27±11 ms) (P=0.0001).They found higher left ventricular ejection fractions in the deferiprone and the desferrioxamine versus the deferasirox group (P=0.010). The cohort of patients treated with oral deferiprone showed less myocardial iron burden and better

global systolic ventricular function compared to the patients treated with oral deferasirox or subcutaneous desferrioxamine.[9]

7. Glickstein et al(2006) conducted a study on action of chelators in iron-loaded cardiac cells: accessibility to intracellularlabile iron and functional consequences They compared the iron chelatorsdeferoxamine,deferiprone, and deferasirox as scavengers of labile iron in plasma and cardiomyocytes at therapeutic concentrations.The effect of deferoxamine at therapeutically relevant concentrations was primarily by elimination of LPI. The rapid accessibility of the oral chelatorsdeferasirox and deferiprone to intracellular labile iron compartments renders them potentially efficacious for protection from and possibly reversal of cardiac damage induced by iron overload.[11]

6.3 AIMS AND OBJECTIVE OF THE STUDY

- To audit the chelation practices in thalassemia day care centre of tertiary care hospital in Punjab.
- To compare outcomes in terms of iron overload across various treatment regimes.

7.0 MATERIALS & METHODS:

This is an observational study to audit chelation practices iron overload in patients with thalassemia will be conducted in the Thalassemia day care centre in the Department of Paediatrics, Dayanand Medical College and Hospital, Ludhiana from (1^{ST} September 2022 to 31st August 2023).

7.1 SOURCE OF DATA: All the transfusion dependent thalassemia children in the age group of 1-18 years with thalassemia and receiving deferasirox,deferiprone or desferal and on follow up in day care centre in the Department of Paediatrics, Dayanand Medical College and Hospital, Ludhiana will be included in the study.

7.2 METHODS OF COLLECTION OF DATA

INCLUSION CRITERIA:

- Patient with transfusion dependent transfusion dependent thalassemia between the age group of 1 -18 years
- Patients who have taken atleast 1 dose of iron chelation.
- Patients who consent for being the part of the study.

EXCLUSION CRITERIA:

- Patients <1 and >18 years of age& patients who donot give consent.

METHOD OF COLLECTION OF DATA:

- All the patients with transfusion dependent thalassemia registered in the centre and received leucodepleted PRBC 15-20 ml/kg every 3-5 weeks to maintain a pretransfusion Hb between 9-10.5 g/dl.
- Patient assessment regarding hemoglobin and transfusion details, socioeconomic details, serum ferritin levels,liver enzymes and serum creatinine were recorded.
- Any adverse effect to iron chelation was also recorded from the patient files/ patient interview.

PARAMETERS OF EFFICACY:

- Serum ferritin levels repeated every 3 months.
- Cardiac MRI T2*
- Liver iron concentration (by MRI T2*)
- Growth[weight/, height/, sexual maturity rate (in >10 years), BMI]

PARAMETERS OF SAFETY (ADVERSE EFFECT GRADING ACCORDING TO CTCAE VER 5)

CTCAE TERM	GRADE 1	GRADE 2	GRADE 3	GRADE 4	GRADE 5
1. RASH	Mild often resolve spontaneously	Moderate often resolve spontaneously and continue treatment without dose adjustment	Severe Rash Interrupt treatment and consider the use of systemic corticoids	-	-
2. PAIN ABDOMEN *Definition*: A disorder characterized by a sensation of marked discomfort in the abdominal region.	Mild pain	Moderate pain; limiting instrumental ADL	Severe pain; limiting self careADL	-	-
3. NAUSEA *Definition*: A disorder characterized by a queasy sensation and/or the urge to vomit.	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition	Inadequate oral caloric or fluid intake; tube feeding, TPN, or hospitalization indicated	-	-
4. VOMITING *Definition*: A disorder characterized by the reflexive act of ejecting the contents of the stomach through the mouth	Intervention not indicated	Outpatient IV hydration; medical intervention indicated	Tube feeding, TPN, or hospitalization indicated	Life-threatening consequences	Death
5. NEUTROPENIA	-	-	ANC <1000/ µl	Life threating consequences urgent intervention indicated	Death
6. THROMBOCYTOPENIA	< LLN – 75000/µl	50000 – 75000/µl	< 25000 – 50000/µl	< 25000/µl	
7. RISE IN SERUM CREATININE	-	-	-	-	-
8. Raised AST/ALT	> 1.5 - 5 ULN	> 5 - 10 ULN	> 10 ULN	-	-
9. VISUAL DEFECTS	-	-	-	-	-
10. AUDITORY DEFECTS	-	-	-	-	-

CLINICAL SIGNIFICANCE:

After this study, we will be able to study the outcome of various chelation regimen followed in various groups of patients.

OUTCOME: After the study we will be able to comparethe outcome of various chelation practices in thalassemia day care centreat tertiary care hospital in Punjab.

STATISTICAL ANALYSIS:

Data will be described in terms of range; mean ±standard deviation (± SD), frequencies (number of cases) and relative frequencies (percentages) as appropriate. For comparing categorical data, Chi square ($\chi 2$) test will be performed and fisher exact test will be used when the expected frequency is less than 5. A probability value (p value) less than 0.05 will be considered statistically significant. All statistical calculations will be done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

Yes,

- SGPT
- SERUM CREATININE LEVELS
- URINE PROTEIN/CREATININE RATIO
- AUDIOMETRY
- OPHTHALMOLOGIC EXAMINATION
- ECHO

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached herewith.

REFERENCES

1. Hoffbrand AV, Taher A, Cappellini MD. How I treat transfusional iron overload. Blood, The Journal of the American Society of Hematology. 2012;120:3657-69.
2. Cappellini MD, Cohen A, Piga A, Bejaoui M, Perrotta S, Agaoglu L et al. A phase 3 study of deferasirox (ICL670), a once-daily oral iron chelator, in patients with β-thalassemia. Blood. 2006;107:3455-62.
3. Shah N, Mishra A, Chauhan D, Vora C, Shah NR. Study on effectiveness of transfusion program in thalassemia major patients receiving multiple blood transfusions at a transfusion centre in Western India. Asian J TransfusSci 2010;4:94‑8.
4. Cappellini MD, Bejaoui M, Agaoglu L, Canatan D, Capra M, Cohen A, et al. Iron chelation with deferasirox in adult and pediatric patients with thalassemia major: efficacy and safety during 5 years' follow-up. Blood, The Journal of the American Society of Hematology. 2011;118:884-93.
5. Glickstein H, El RB, Link G, Breuer W, Konijn AM, Hershko C, et al. Action of chelators in iron-loaded cardiac cells: accessibility to intracellular labile iron and functional consequences. Blood. 2006;108:3195-203.
6. Cooley TB, Lee P. Series of cases of splenomegaly and peculiar changes in the bones. Trans. Am. Pediat. Soc. 1925;37:29-30.
7. Shah R, Trehan A, Das R, Marwaha RK. Serum ferritin in thalassemia intermedia. Indian Journal of Hematology and Blood Transfusion. 2014;30:281-5.
8. Mohanty D, Colah RB, Gorakshakar AC, Patel RZ, Master DC, Mahanta J. Prevalence of β-thalassemia and other haemoglobinopathies in six cities in India: a multicentre study. Journal of community genetics. 2013;4:33-42.
9. Pepe A, Meloni A, Capra M, Cianciulli P, Prossomariti L, Malaventura C, et al A. Deferasirox, deferiprone and desferrioxamine treatment in thalassemia major patients: cardiac

iron and function comparison determined by quantitative magnetic resonance imaging. haematologica. 2011;96:41.

10. Cohen AR, Glimm E, Porter JB. Effect of transfusional iron intake on response to chelation therapy in β-thalassemia major. Blood, The Journal of the American Society of Hematology. 2008;111:583-7.
11. Glickstein H, El RB, Link G, Breuer W, Konijn AM, Hershko C, et al. Action of chelators in iron-loaded cardiac cells: accessibility to intracellular labile iron and functional consequences. Blood. 2006;108:3195-203.
12. Cooley TB, Lee Physiology of bone Physiopathology of Bone Modifications in -Thalassemia Trans. Am. Pediat. Soc. 1925;37:29-30.
13. Shah R, Trehan A, Das R, Marwaha RK. Serum ferritin in thalassemia intermedia. Indian Journal of Hematology and Blood Transfusion. 2014;30:281-5.
14. Hassan MA, Tolba OA. Iron chelation monotherapy in transfusion‐dependent beta‐thalassemia major patients: A comparative study of deferasirox and deferoxamine. Electron Physician 2016;8:2425-31.
15. Cappellini MD, Bejaoui M, Agaoglu L, Canatan D, Capra M, Cohen A, et al. Iron chelation with deferasirox in adult and pediatric patients with thalassemia major: efficacy and safety during 5 years' follow-up. Blood, The Journal of the American Society of Hematology. 2011;118:884-93.
16. Davis BA, Porter JB. Long-term outcome of continuous 24 hour deferoxamine infusion via indwelling intravenous catheters in high-risk beta thalassemia.Blood. 2000;95:1229-36.
17. Taher A, Sheikh-Taha M, Sharara A, Inati A, Koussa S, Ellis G, et al Safety and effectiveness of 100 mg/kg/day deferiprone in patients with thalassemia major: a two-year study. Actahaematologica. 2005;114:146-9.

18. Cappellini MD, Cohen A, Piga A, Bejaoui M, Perrotta S, Agaoglu L, et al A phase 3 study of deferasirox (ICL670), a once-daily oral iron chelator, in patients with β-thalassemia. Blood. 2006;107:3455-62.

PROFORMA

S. No. TDCC NO. DATE:

NAME AGE: SEX:

MRD NO: ADMN. NO:

ADDRESS:

ANTHROPOMETRY	ACTUAL	EXPECTED	REMARKS
WEIGHT (KG)			
HEIGHT/LENGHT (CM)			
BMI			

Fetal hemoglobin (HbF)

FATHER	MOTHER	BROTHER	SISTER

MODIFIED KUPPUSWAMI SCALE:

BLOOD GROUP:

VIRAL MARKERS:

AGE AT ENROLLMENT	AGE AT DIAGNOSIS OF THALASSEMIA	AGE AT STARTING OF IRON CHELATION	DATE OF STARTING OF IRON CHELATION

- COMPLIANT (>90%): YES/NO
- HISTORY OF SPLENECTOMY- YES/NO
- MENINGOCOCCAL VACCINE: YES/NO
- PNEUMOCOCCAL VACCINE LAST DOSE

Signature of Candidate **Signature of Supervisor**

ANNUAL TRANSFUSION REQUIREMENTS (ml/kg/yr):

Y0	Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10

Y11	Y12	Y13	Y14	Y15	Y16	Y17	Y18	Y19	Y20	Y21

AVERAGE HEMOGLOBIN: (Formula Used Mean = Sum of Terms/Number of Terms):

Y0	Y1	Y2	Y3	Y4	Y5	Y6	Y7	Y8	Y9	Y10

Y11	Y12	Y13	Y14	Y15	Y16	Y17	Y18	Y19	Y20	Y21

SERUM FERRITIN LEVELS:

SF0	SF 1	SF 2	SF 3	SF 4	SF 5	SF 6	SF 7	SF 8	SF 9	SF 10

SF11	SF 12	SF 13	SF 14	SF 15	SF 16	SF 17	SF 18	SF 19	SF 20	SF 21

Signature of Candidate **Signature of Supervisor**

SEXUAL MATURITY RATE (ACCORDING TO TANNER'S STAGING)

Table 1

Tanner Stage	Breasts	Pubic Hair	Growth	Other
1	Elevation of papilla only	Villus hair only	2-2.4 inches per year	Adrenarche and ovarian growth
2	Breast bud under the areola, areola enlargement	Sparse hair along the labia	2.8-3.2 inches per year	Clitoral enlargement, labia pigmentation, growth of uterus
3	Breast tissue grows but has no contour or separation	Coarser hair curled pigmented covers the pubes	3.2 inches per year	Axillary hair, acne
4	Projection of areola and papilla, secondary mound formation	Adult hair, does not spread to the thigh	2.8 inches per year	Menarche and development of menses
5	Adult-type contour, projection of papilla only	Adult hair, spreads to the medial thigh	Cessation of linear growth	Adult genitalia

Table 2

Tanner Stage	Genitalia	Pubic Hair	Growth	Other
1	Testes <2.5 cm	Villus hair only	2.0-2.4 inches per year	Adrenarche
2	Testes 2.5-3.2 cm Thinning and reddening of the scrotum	Sparse hair at penis base	2.0-2.4 inches per year	Decreases in body fat
3	Testes 3.3-4.0 cm Increase of penis length	Thicker curly hair spreads to the pubis	2.8-3.2 inches per year	Gynecomastia, voice break, increased muscle mass
4	Testes 4.1-4.5 cm, penis growth darkening of scrotum	Adult hair does not spread to thighs	4.0 inches per year	Axillary hair, voice change, acne
5	Testes >4.5cm, adult genitalia	Adult hair spreads to medial thigh	Deceleration, cessation	Facial hair, muscle mass increases

DRUG USED:

	USED (Yes/ No)	MEAN DOSE (mg/kg)	DURATION OF EXPOSURE (Date of Starting – Date of Stopping = NO. of Months)
DEFERASIROX			
DEFEROXAMINE			
DEFERIPRONE			

DOSE REDUCTION NEEDED: YES/NO

CAUSE:

Signature of Candidate **Signature of Supervisor**

CARDIACMRI T2: (IN>10 YEARS OF AGE)

YEAR OF STUDY	INTERPRETATION

LIVER IRON CONCENTRATION MRI T2: (IN>10 YEARS OF AGE)

YEAR OF STUDY	INTERPRETATION

Signature of Candidate **Signature of Supervisor**

PARAMETERS OF SAFETY (ADVERSE EFFECT GRADING ACCORDING TO CTCAE VER 5)

CTCAE TERM	GRADE 1	GRADE 2	GRADE 3	GRADE 4	GRADE 5
1. RASH	Mild often resolve spontaneously	Moderate often resolve spontaneously and continue treatment without dose adjustment	Severe Rash Interrupt treatment and consider the use of systemic corticoids	-	-
2. PAIN ABDOMEN *Definition*: A disorder characterized by a sensation of marked discomfort in the abdominal region.	Mild pain	Moderate pain; limiting instrumental ADL	Severe pain; limiting self careADL	-	-
3. NAUSEA *Definition*: A disorder characterized by a queasy sensation and/or the urge to vomit.	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition	Inadequate oral caloric or fluid intake; tube feeding, TPN, or hospitalization indicated	-	-
4. VOMITING *Definition*: A disorder characterized by the reflexive act of ejecting the contents of the stomach through the mouth	Intervention not indicated	Outpatient IV hydration; medical intervention indicated	Tube feeding, TPN, or hospitalization indicated	Life-threatening consequences	Death
5. NEUTROPENIA	-	-	ANC <1000/ µl	Life threating consequences urgent intervention indicated	Death
6. THROMBOCYTOPENIA	< LLN – 75000/µl	50000 – 75000/µl	< 25000 – 50000/µl	< 25000/µl	
7. RISE IN SERUM CREATININE	-	-	-	-	-
8. Raised AST/ALT	> 1.5 - 5 ULN	> 5 - 10 ULN	> 10 ULN	-	-
9. VISUAL DEFECTS	-	-	-	-	-
10. AUDITORY DEFECTS	-	-	-	-	-

Signature of Candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I…….D/o, W/o, S/o……..…… am willing to participate in the study **"AN OBSERVATIONAL STUDY OF IRON CHELATION PRACTICES IN THALASSEMIA DAY CARE CENTRE OF A TERTIARY CARE HOSPITAL IN PUNJAB"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

…… ……

Signature of the Witness Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य "**AN OBSERVATIONAL STUDY OF IRON CHELATION PRACTICES IN THALASSEMIA DAY CARE CENTRE OF A TERTIARY CARE HOSPITAL IN PUNJAB"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____	_____
गवाह के हस्ताक्षर	रोगी के हस्ताक्षर/अंगूठे का निशान
नाम:	नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

“AN OBSERVATIONAL STUDY OF IRON CHELATION PRACTICES IN THALASSEMIA DAY CARE CENTRE OF A TERTIARY CARE HOSPITAL IN PUNJAB” ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ